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Fiftieth Anniversary of the Discovery of Radium

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Marie Curie

Pierre Curie

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 60 DECEMBER, 1948 No. 6

FIFTY YEARS OF RADIUM*

By EDITH H. QUIMBY, Sc.D.

College of Physicians and Surgeons, Columbia University

NEW YORK, NEW YORK

RADIUM was discovered fifty years ago. In the succeeding half century it has played an important triple role in medicine, science, and industry. It would have been difficult or impossible to forsee the significance of the discovery; it was regarded at the time mainly as a scientific curiosity. Nobody then had the vision to anticipate that it would open up whole new fields of medical and scientific research,—to say nothing of international relations.

We are today commemorating the discovery of radium; in so doing we pay tribute to the discoverers, Marie and Pierre Curie, and we may well recall a little of their story. The production of x-rays had been announced by Roentgen at the end of 1895, and immediately physicists everywhere had started to duplicate and extend his experiments. Early x-ray tubes all fluoresced brilliantly, and it was natural to associate this fluorescence with the new rays. Various workers suggested the possibility that naturally fluorescent minerals might also give off invisible penetrating radiations, and a few sporadic efforts were made to find such a phenomenon. Becquerel, in Paris, undertook a systematic investigation of the problem, testing a large variety of minerals and compounds. He discovered that compounds of uranium which were fluorescent did actually emit invisible radiations, which darkened a photographic plate. Furthermore, to his surprise, he found that it was not at all necessary for the material to be fluorescing or phosphorescing in order for it to produce this effect. Becquerel announced this discovery in the spring of 1896 (only a few months after Roentgen's first paper) and went on studying the phenomenon during that year. He observed that, in addition to their photographic effect, these rays could discharge an electroscope. He also found that all compounds of uranium emitted them, that is, the radiation was a property of uranium, regardless of its chemical combination.

It was at this point that Mme. Curie entered the picture. A shy, but talented and studious Polish girl, Marie Sklodowska, had grown up in Warsaw, while it was under oppressive Russian domination. All Polish national feeling was strongly suppressed and Polish schools were severely limited. Her elementary and secondary education

* An Address delivered at the Annual Banquet at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

was acquired partly in private and partly in government schools. Afterward she worked as a governess, meantime striving to carry her education to the point where she might to go Paris and study at the Sorbonne. This she finally achieved in 1891, at the age of twenty-four. Within three years she had graduated as a licencié in physics and mathematics, and was ready to begin work for her doctorate. About that time she met Pierre Curie; they were married in 1895. During the next two years they worked together in his laboratory, so that she acquired facility in experimental research, while seeking a suitable problem for her doctor's thesis. She became interested in Becquerel's work, and decided to study the radiations which he had discovered. It was of interest to see whether any substances besides uranium emitted them, and it was desirable to make quantitative measurements of their intensity. She quickly demonstrated that the amount of activity in a uranium compound was exactly proportional to the amount of uranium there; in other words, it was a definite property of the uranium atom. To see whether other atoms also gave off radiations, she studied all the elements then known, and found them emitted only by uranium and thorium. She coined the word *radioactivity* to describe or define the phenomenon.

During the course of her research she examined not only elements and compounds, but also a number of natural ores or minerals. To her great surprise, she found that certain of these, containing uranium, were much more active than could be accounted for by their content of this metal. She was obliged to believe that these ores must contain very small quantities of some element, hitherto unknown, which was much more strongly radioactive than uranium itself. She had, as she says, a passionate desire to verify this hypothesis as rapidly as possible. And her husband, also keenly interested, abandoned his own research (as he thought for the time being) to join with her in the investigation.

They chose to work with pitchblende, a uranium ore about four times as radioactive as the element itself, and whose composition was quite well known. They used standard chemical procedures,—pulverization, solution, precipitation, fractional crystallization—but at every step they tested the radioactivity of each portion. They soon recognized that the new substance was concentrating in a regular way—and then presently they discovered that they had not one, but two new radioactive elements. One, staying with bismuth in all the reactions, was identified first, it was announced in July 1898, and named polonium, in honor of Mme. Curie's native country. The other, associated with barium, was separated later; it was announced that December with the name of radium, to indicate its very intense activity.

These first separations involved only minute quantities of the new elements, in order to find out anything about them beyond their radioactivity, it was necessary to isolate measureable amounts. This meant subjecting many kilograms of the ore to careful chemical treatment, since its radium content was so minute—not more than one part in several million.

They had no money, no suitable laboratory, no personal help,—as she says in her autobiographical notes "it was like creating something out of nothing." They wanted to isolate the radium from a considerable amount of pitchblende, but they could not even afford to buy the ore. However, they knew from their experiments that in the commercial treatment of pitchblende in the Bohemian mines, radium must have been left in the residues. Fortunately these residues had not been scattered, but had been piled in a heap outside the plant. They were there quite valueless, and the Austrian government gave them some, and later sold them several tons at a low price. From this material was prepared all the radium Mme. Curie had in her laboratory for many years.

They were allowed to carry on their work in an old shed with a leaky glass roof, cold

in winter, hot in summer; they had only the most primitive of laboratory equipment. But there they spent their entire time for the next two years, occupied both with chemical research and with gradually obtaining appreciable amounts of radioactive material and studying the radiations. After that period of joint work, they divided their efforts. Mme. Curie continued with chemical experiments leading to the preparation of pure radium salts; her husband went on studying the properties of radium.

During this time they were leading a quiet but happy family life. Their first daughter, Irene (destined to become a famous scientist in her own right) had been born in 1897, in 1904 came the second one, Eve (who has had a distinguished musical and literary career). In 1900 both husband and wife received good academic appointments, so that their financial strain was eased and they were able to have better laboratory facilities.

In 1903 the Curies and Becquerel jointly were awarded the Nobel prize for physics. Other prizes and awards followed and it looked as though a brilliant future stretched before them. Then in 1906 Pierre was suddenly killed by being struck by a truck. This was a catastrophe, both to the family and to the scientific world. At first Mme. Curie thought she could not go on, but of course, as a true scientist, she was bound to. Presently she was offered her husband's professorship at the Sorbonne, and there she carried on her work.

In 1907 she prepared a small quantity of very pure radium chloride, with which she made an accurate determination of the atomic weight of radium. In 1910 she isolated the metal. This is a delicate operation, and one attended with danger of loss of radium. Since the substance is never used in the metallic state, it is not a procedure to be frequently repeated, and actually it has since been done seldom if ever. In 1911, at the request of an international commission, she undertook to prepare an accurate standard of a carefully weighed quantity of pure radium salt. This is in the International Bureau of Weights and Measures at Sèvres, near Paris, and all other standards in all countries have been established by comparison with this. In that same year she was awarded a second Nobel prize, this time alone,—the only person to have been thus honored.

When war came in 1914, she plunged into the organization of radiologic services in the military hospitals. After helping to equip the numerous new institutions that were established all over France, she conceived and put into action a radiologic field car, containing a complete radiographic unit. It was such a success that twenty of them were finally put into service at the front. During this time she made many trips to various army zones, and was unsparing of herself in the actual labor of installing equipment and training personnel.

After the war she devoted herself to the newly established Radium Institute, where both laboratory and medical work were carried out with radium. In 1921 the women of America presented her with a gram of radium for her own scientific research. She came to the United States to receive it, and incidentally many scientific and academic honors. Though always tired and often ill, her years of hard labor and her considerable exposure to radium having left their mark, she continued to direct her laboratory to the time of her death in 1934.

The Curies never accepted any material profit as the result of their discoveries. They took out no patents nor did they sell the radium they extracted. They were often in straitened financial circumstances, even when medals and decorations were being awarded to them. Had they so chosen they could doubtless have capitalized on their achievements, after the discovery of radium had become known, and have consequently lived in greater ease. But theirs was the true scientific spirit. All their discoveries and methods were freely published and available to anyone. All their work was for the unselfish purpose of in-

creasing the sum total of human knowledge,—one wonders what they would have thought if they could have seen where that knowledge would lead.

It would have been impossible, fifty years ago, to predict, or even to imagine the consequences of their work. The discovery of radioactive substances has led to astonishing results in medicine, in physics, chemistry, biology, in business, and in international relations.

The medical use of radium developed from a minor accident. Becquerel carried a glass tube containing radium salt in his vest pocket, and was surprised to find a sore, like a burn, appear on his abdomen. Pierre Curie deliberately produced a similar burn on his arm; this demonstration of the biological effect of the radiation led to animal experiments and to the suggestion of its use in treatment of certain skin diseases. The first radium for medical use was loaned by the Curies to Danlos, at the St. Louis Hospital in Paris. After about three years trial, he published reports on its usefulness in a limited field. In 1906 Wickham and Degrais established in Paris a center for the study of radium therapy, under the name of the Biological Laboratory of Radium, with Dominici in charge of the clinical work. Here the uses of filtration and of cross-fire were promptly discovered and other improvements made in technic.

In England the Radium Institute of London was formed about the same time, and in America various doctors obtained radium for use in therapy. Dr. Robert Abbe of New York was apparently the first person to implant radium directly into a tumor, in 1905 but intracavitary use in gynecology preceded this in France.

Mme. Curie had discovered that radium gave off a radioactive gas, which she called Emanation—it is now called radon. This has all the biological effects of radium itself, and it began to be employed in therapy, both in France and in America. The precious radium—and at that time it was extremely valuable,—could be kept in a safe, with no danger of loss, theft, or breakage, and the gas regularly drawn off. Such installations were made at Memorial Hospital in New York, the Howard Kelly Hospital in Baltimore, the Huntington Hospital in Boston, and eventually a considerable number of others. At the Memorial Hospital, Janeway and Failla developed methods of implanting tubes of radon directly into tumors, first bare glass ones, and later those of gold, which filtered out the less penetrating rays responsible for most of the local necrosis formed around the glass ones. The advantage of this type of therapy, was that, since the radon lost its activity gradually over a period of a month, the little containers, or "seeds" did not need to be removed, as had to be done with needles actually containing radium. This simplified the necessary surgical technic.

However, since the great decrease in the price of radium, and the manufacture of a variety of small removable radium needles, some of the advantages of permanent implants are not so great. With development of various special types of x-ray therapy, the use of radium or radon in superficial lesions has become largely outmoded. The result has been that most of the radon plants in this country have been dismantled, the radium put into permanent containers, and commercial companies depended upon for the supply of radon when it is desired.

Because the gamma rays of radium are much more penetrating than the x-rays which are usually available for therapy, they offer a means for treating deep-seated tumors. As production of radium became considerable and its price somewhat reduced, several institutions acquired relatively large amounts which they used in large "packs" or "bombs," the radium being at several centimeters distance from the skin. This "Telecurie Therapy" found enthusiastic advocates in France, Belgium, Sweden, England, and to a less extent, in America. Treatments must be very long, and even with large amounts of radium, depth doses are not very good because the radium-skin distances used can be only a few centimeters. With the development of

x-ray machines operating at one or several million volts, the advantages of telecurie therapy cease to exist and most of the large units in this country have been broken up.

But radium still possesses its unique place in intracavitary and interstitial therapy. Here its advantages are great and unquestioned. It may be superseded by some of the artificial radioactive elements, but that is not evident at present.

No account of the history of radium would be complete without some details as to its commercial production. The first preparations of nearly pure radium salt were put on the market by Dr. Giesel, of the Chininfabrik Braunschweig; he first sold radium bromide at one English pound per milligram. Later it went to 12 times this, but this firm never really made a business of radium supply. The idea of a radium factory was first conceived by a Frenchman, Armet de Lisle, and in cooperation with the Curies he actually started one, in 1902, which supplied the early French demands. He also founded, in 1906, a laboratory for clinical study, providing it with radium, and he subsidized the first special publication devoted to radium.

Other extraction plants developed in Europe. The source of their ore was at first the Bohemian pitchblende, of which the Austrian government had made a monopoly. Then radium was discovered in a Colorado ore called carnotite and for a time this ore was shipped to Europe.

In 1911 the Standard Chemical Company was formed by Mr. Joseph Flannery of Pittsburgh, to separate radium from carnotite in the United States, and their first radium was put on the market in 1913. This was a completely new industry; it was not possible to get any of the few men who had been trained in this field in Europe, so the whole procedure had to be developed from the beginning. The Colorado carnotite was a much poorer ore than pitchblende. Whereas the latter had a gram of radium in 4 or 5 tons, in the former, 400 or 500 tons were necessary—and each of these 400 or 500 had to be hand picked out of a much larger mass of dirt, and rock. This was done in the field. The crude ore was carried out by burros to a central concentration plant where it was pulverized, sacked, and sent to the Pittsburgh plant for refinement. In reducing and purifying one gram of radium from 500 tons of ore, it was necessary to use 10,000 tons of distilled water, 1,000 tons of coal and 500 tons of chemicals. It is no wonder that this gram of radium sold for $120,000, —and it had a volume less than a thimble full.

About the same time that the Standard Chemical Company got under way, Dr. Howard Kelly, of Baltimore, brought some radium from Europe. He was very much pleased with his clinical results, and became interested in producing the material in America. Accordingly, he joined forces with Dr. James Douglas of New York, a distinguished mining engineer, and the U.S. Bureau of Mines, and formed the National Radium Institute to extract radium from carnotite. Dr. Kelly and Dr. Douglas provided the capital, and the Bureau of Mines developed the processes and supervised the work. The agreement lasted from 1914 to 1917, during which time about 8.5 gm. of radium were extracted, most of which was divided between the Kelly Hospital in Baltimore, and the Memorial Hospital in New York. Meantime several other commercial companies came into the field. Some were short lived, but two, the Radium Company of Colorado, and the United States Radium Corporation, as well as the Standard Chemical Company, were stable as long as American ore was the world's chief source of radium, namely until 1923.

Much richer ores had been found in the Belgian Congo as early as 1913, but during the war nothing was done about developing them. However, after 1920, the Union Minière du Haut Katanga, and its subsidiary, the Radium Belge, began to produce radium. This ore, mined in the Congo, was packed in sacks and carried

overland 1,600 miles to the seacoast and there shipped to Belgium for purification. With ores forty times as rich as carnotite and with cheap labor, the cost dropped to $70,000 a gram. The radium industry in America could not compete and was practically wiped out over night; the American concerns arranged to market the Belgian product.

This had a monopoly for a number of years, and maintained its price around $70,000 a gram. Then about 1930, very rich radium ores were found in the Great Bear region of Northern Canada.

It appears that large uranium finds are in remote parts of the earth,—first the high ranges of the Rocky Mountains, then the tropic wilderness of central Africa, and finally the frozen north. And it is literally frozen for a considerable part of the year. The ore is partially reduced at the mines, and the concentrates flown out by plane for the final operations. The Canadian Radium and Uranium Corporation was formed to exploit this material. Their competition brought the price down to about $35,000 a gram and it has remained in that neighborhood. Canadian and Belgian radium now supply the world's market. American companies have arrangements to sell their products, but Colorado ore is no longer used for radium production,—it is now under the control of the Atomic Energy Commission.

Developments in physics and chemistry, as the result of the discovery of radium, have proceeded at a constantly accelerating pace. From the first discovery, Pierre Curie was occupied with studying the phenomena connected with radioactivity, and trying to explain them. Debierne, Danne, Laborde, and others were associated with him in some of these investigations. One of their most striking discoveries was the spontaneous production of heat by radium. With no alteration in appearance, a radioactive salt produces each hour sufficient heat to melt its own weight in ice.

This and other phenomena attracted the attention of other physicists, and in particular of Rutherford and his associates at the Cavendish Laboratory in Cambridge. He demonstrated that not all the radiations from radioactive substances were alike; by 1899 he had identified the two types which are called alpha and beta. Villard almost immediately discovered the still more penetrating gamma rays and before the beginning of the century a number of papers had appeared concerning the characteristics and properties of the different rays.

It was promptly recognized that the alpha and beta rays consisted of matter expelled from the atoms themselves. Evidently if this were true, the atoms could not be the hard, solid, indivisible pellets they had been assumed to be. The actual demonstration as to their nature came when Rutherford set a young student, Marsden, to study the scattering of alpha particles as they traversed thin metal films. Contrary to expectation some particles were found to be scattered directly backward. Rutherford's own description of his reaction to this news is graphic. He says "It was quite the most incredible event that has ever happened to me in my life. It was almost as incredible as if you fired a 15 inch shell at a piece of tissue paper and it came back and hit you. I saw that it was impossible unless you took a system in which the greater part of the mass of the atom was concentrated in a minute nucleus." Thus arose the concept of the solar system type of atom which is accepted today. The present picture of the structure of the atom, with orderly increase in nuclear charge and in number of orbital electrons from element to element was developed from the work of many, of whom Mosley, Chadwick, and Bohr are outstanding. When this conception was accepted it became evident that in a radioactive transformation somehow a bit of the nucleus was expelled; this meant a change of the atom into an atom of another element.

The naturally radioactive elements are those with very heavy nuclei. Rutherford believed that these nuclei had a complicated

structure which was inherently unstable, and that atoms of the lighter elements, with simple stable nuclei, might be made to disrupt if some sort of projectile could be fired into them. He actually succeeded in doing this, by firing alpha particles into nitrogen nuclei, and making them eject something which was found to be a hydrogen nucleus. Thus it was proven that one of the constituents of nitrogen nuclei was this hydrogen nucleus, a little particle, of mass one on the atomic scale and having a single positive electric charge. Other elements were promptly attacked by the same weapon and many of them could be broken down, emitting this same hydrogen particle, to which was given the name "proton." Then a second component was found, identified by Chadwick as having the same mass as the proton, but no charge at all. This was named a "neutron." It is now believed that all atomic nuclei are built up of combinations of these two particles, while travelling around each nucleus in a series of orbits are just the right number of negative electrons to balance the positive electric charge on the nuclear protons.

Of course many physicists eagerly verified and extended the work of Rutherford and his group. Among the most enthusiastic of these were Irene Curie, the older daughter of Marie and Pierre Curie, and her husband, Frederick Joliot. As a scientific team, following the illustrious example of her parents, they have done brilliant work and have themselves received the Nobel prize for the discovery of artificial radioactivity. That is, they found that sometimes when they performed experiments bombarding certain elements with alpha particles, after the bombardment stopped, the target material continued to emit radiation for a time. This activity decreased gradually in the same manner as that from radioactive elements, in fact the target had been made truly radioactive. They announced their discovery in 1934, describing radioactive boron and aluminium. Since then, radioactive forms of every element have been made. These different kinds of atoms of the same element are called *isotopes*, they have the same number of nuclear protons and of orbital electrons but slightly different numbers of nuclear neutrons. They are of course actually the same element, isotopes are chemically inseparable.

Every radioactive disintegration results in an emission of a relatively very large amount of energy. During the years after the discovery of artificial or induced radioactivity, there was much speculation as to the possibility of the development of a chain reaction whereby one disintegration could set off another, and that another and so on, without the need of supplying any more external bombarders. Such a chain could serve as a source of energy for a heat generator, or, if it could be compact enough and fast enough, a bomb.

This was mere speculation for some years and then the chain reaction was actually found. When one isotope of uranium is bombarded with neutrons, it disintegrates and in its disintegration emits neutrons, which can enter other atoms, making them disintegrate, and so on.

This was discovered in 1939. A few scientists, in America, immediately recognized the military possibilities of the discovery, and tried to convince first the Navy, and then the Army of its value, but it was not until they made a direct appeal to President Roosevelt that actual work in that direction was started. The world knows the results.

Thus along the pathway of scientific research, which started a half century ago in a small investigation of a phenomenon which had no imaginable practical value, humanity has come to a crisis. Where it will go depends on itself. But humanity really means a lot of individuals,—rich and poor, well-fed and hungry, peaceable and quarrelsome, generous and selfish, wise and injudicious. There are true differences of opinion as to what is best for peoples and nations,—and there is demagoguery and hysteria; there are threats and violence and fear. The possible extension of this particular scientific pathway

can lead to great peacetime good,—or it can lead to most horrible war. This little talk is history, not prophecy. But it must be evident that only the working out of a just and stable peace, with the recognition of all men's rights to life with certain basic freedoms, and some firm, super-national, law-abiding order, can make a world in which atomic energy can properly be used.

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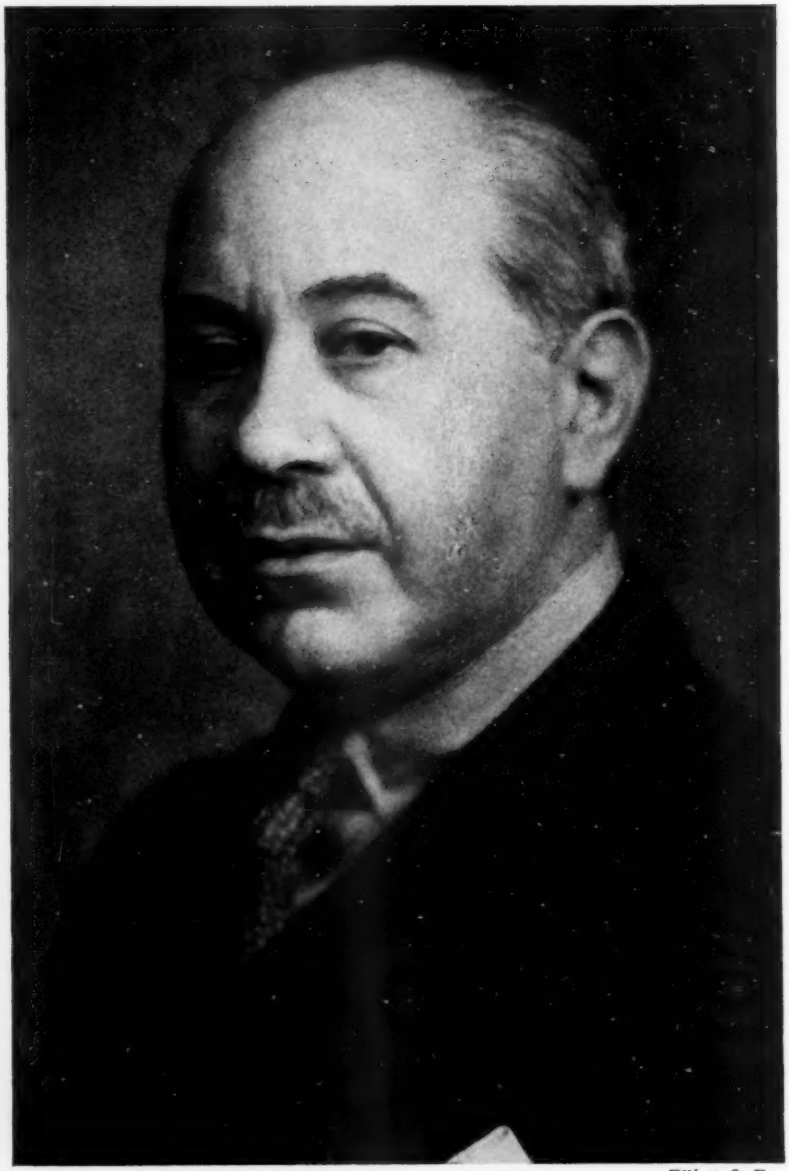

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SIR STANFORD CADE, K.B.E., C.B., F.R.C.S.

JANEWAY LECTURER, 1948

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THE ACHIEVEMENT OF RADIUM IN THE FIGHT AGAINST CANCER

JANEWAY LECTURE, 1948*

By SIR STANFORD CADE, K.B.E., C.B., F.R.C.S.

Surgeon, Westminster Hospital, Mount Vernon Hospital and the Radium Institute

LONDON, ENGLAND

WHATEVER the future holds in store in the way of treatment of cancer, be it isotopes or endocrines, chemotherapy or any form of ionizing energy, Radium will remain a landmark in the therapeutics of neoplasms and the second battle victory, Surgery being the first in point of time, on the road to the conquest of this foe of living beings.

It pleases me to think that Janeway, whose memory we honor today as an American pioneer in the clinical use of Radium, may perhaps smile benevolently on this gathering, as for the first time since the inception of this lecture in 1933, it is delivered by a non-American. My first duty is to thank the American Radium Society for the honor in offering me this year's Janeway Lectureship and it is a difficult task to express adequately my sense of gratitude to your President and Selection Committee and to convey to you my appreciation of this distinction.

If we pursue this flight of fancy and imagine what impression this, the thirteenth Janeway Memorial Lecture, might have had on the man whom it eponymously honors, it is necessary to say something about Janeway himself. He was pursued by ill health and he knew personally what it is to suffer from a neoplasm. He was trained as a surgeon and, by special individual effort, acquired the necessary knowledge of physics to use radium both safely and efficiently. He published forty-one scientific papers. In England his name is a household word amongst surgeons in connection with the operation of gastrostomy,[13] which he described in 1913 and which has stood the test of time as a sound surgical procedure. His greatest work was published after his death as "The Second Radium Report from the Memorial Hospital."[14]

With this background, I thought it right to devote this lecture to the "Achievement of Radium in the Fight Against Cancer," and to attempt a review of the whole field and not of any single or isolated achievement. This is perhaps a suitable occasion as it is the Fiftieth Anniversary of the discovery of Radium. Half a century is a short period, yet radium has achieved much; like all great additions to knowledge it developed by leaps and bounds. In the past ten years it has suffered loss of popularity with the development of roentgen therapy. This swing of the pendulum is yet a further reason for a review of what radium has achieved. The debt of science to radium can be subdivided into three broad groups—physical, biological and therapeutic. I will endeavor to review briefly these three achievements with special emphasis on the therapeutic side.

One year after the discovery of x-rays by Röntgen, a French physicist, Henry Becquerel, communicated to the French Academy of Science his observation that one of the natural elements, uranium, was spontaneously and continuously emitting radiation which, like roentgen rays, could penetrate matter. It took Marie Curie and her husband, Pierre, two years to isolate the new element—radium. The exact date of their first communication is December 26, 1898. So in an obscure shed, a frail young woman, working in poor conditions, discovered, isolated and studied some of the

* The thirteenth Janeway Lecture, delivered at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Illinois, June 20–22, 1948.

properties of a new substance, the importance of which to the safety of future generations of mankind can hardly be overestimated. It can be compared in magnitude to the first conquest of fire by the ancestors of man in prehistoric time. And yet it was less than a brief fifty years, a mere fraction in the history of mankind, from the discovery of radium by Marie Curie in Paris to the dropping of the first atomic bomb by the American Army Air Force on Hiroshima.

The credit of the discovery of roentgen rays belongs to Germany, that of the discovery of radium to Poland and France. I think it is right to say that Britain may claim the first place in the systematic development of the laws of radioactive transformation. It was Rutherford in 1899 who first identified the alpha and beta particles of radium. This led him to draw accurate conclusions as to the structure of the atom and the mathematical proof of the existence of the nucleus of the atom. In 1919 he showed experimentally that a charged alpha particle could collide with the nucleus of an atom of nitrogen and break it up into two other atomic species, a step towards the artificial disintegration of an atom. Lord Rutherford is to radiotherapy what Lord Lister is to surgery. He deserved and received many honors, amongst them an LL.D. from the University of Pennsylvania and from the University of Wisconsin, a Ph.D. from Yale University and a D.Sc. from the University of Toronto; he was also made an honorary member of five American Scientific Societies. With the death of Rutherford in 1937, a great epoch in science came to an end. His biographer, Professor A. G. Eve, compares him to Galileo and Newton, who began and ended one such famous epoch—the discovery of the mechanism of the Universe; to Faraday and Maxwell who achieved the foundations of electricity, and to Einstein and Planck who opened the doors of relativity and of quanta.

Mention must also be made of Sir James Chadwick who, working with Rutherford at the Cavendish Laboratory, Cambridge, discovered the existence of the neutron; this discovery led to a complete revision of modern atomic physics and to the birth of nuclear physics. Thus the discovery of Radium and of the Laws of Radioactivity altered our conception of physical matter; The Law of Conservation of Mass and the Law of Conservation of Energy no longer held good. It was Marie and Pierre Curie's daughter Irene and her husband Joliot whose further contributions to the rapid advances of the new science resulted in the production of artificial forms of some radioactive substances. In all three fields—physics, biology and therapeutics—the Janeway Lectures of the past can be usefully used as landmarks in the progress made. This also gives one the opportunity of paying tribute to American pioneers both physicists and clinicians, as well as to those in Great Britain, France and Scandinavia who have contributed to the development of radium therapy.

PHYSICS

The application of radium to the treatment of disease resulted in a need of a unit of measurement of radiation and in the development of a new specialist, the "hospital physicist." In America, two past Janeway lecturers stand out in the front rank of such hospital physicists—Failla[8] and Edith Quimby.[22] Their contribution to the fight against cancer is accuracy in the clinical use of radium, measurement of tissue dose, dosage rate and the correlation of these with the biological effects. The establishment of the roentgen as a unit first in the measurement of roentgen rays and subsequently in that of gamma rays of radium produced further problems, as there is a difference between the two which to the clinician is quite obvious. On our side of the Atlantic, tribute must be paid to Professor Russ and Professor Hopwood—the first two to occupy the position of hospital physicist—to Mayneord, to Gray and to Wilson who by the intensive study of measurements of gamma rays raised the pres-

tige of British hospital physicists in the development of both interstitial and teleradium therapy. To Paterson and Parker of Manchester, we owe a simple method of dose measurement which has been adopted by all radium centers in Great Britian. To quote Edith Quimby—"in a period of twenty years, accuracy has evolved from chaos and we are now concerned with a detail in accuracy undreamed of a few years ago." Physicists have thus by close collaboration with clinicians, brought us nearer to solution of the problems of Science applied to Medicine. The weapon which brought them together is Radium.

BIOLOGY

The biological effects of radiation attracted the attention of pathologists, clinicians and biologists from the earliest days of radiation. The classical studies of Bohn[2] (1903), Perthes[19] (1904), Bergonié and Tribondeau[1] (1904), Dominici[5] (1907), Price-Jones and Mottram[20] (1914) laid the foundation of radiobiology. The key to the treatment of cancer by radium and roentgen rays is the variation in response of normal and malignant tissues to the effects of ionizing energy. The term radiosensitivity can be defined as the relative susceptibility of living cells to a given quantity of ionizing energy. It is the work of Regaud and Lacassagne, of Ewing, of Packard, of Mottram and the tissue culture studies initiated by Strangeways and so brilliantly continued by Canti, Spear and their collaborators at the Strangeways Laboratories, Cambridge, and many others, which have thrown light on the processes which affect radiosensitivity. The main factors can be subdivided into those related to normal physiological processes, to alterations in environment and those in relation to the physical conditions of irradiation. The normal physiological processes include mitosis, stage of embryological development and the type of cell. The factors dependent upon environment are those of metabolism, sepsis, anemia and secretory activity. The most flexible factors are those in relation to the physical conditions of irradiation: time factor, intensity, dosage rate, wavelength and the effects of previous irradiation. Side by side with biophysics, there developed in the last fifty years a new branch of biology—radiobiology. A vast amount of experimental work resulted in a better understanding of the pathology of tumors, a separation of neoplasms according to their degree of response to radiation. Thus radium has played an important part in the advances of other branches of medicine besides therapy, especially in pathology. Soon it became obvious that radiosensitivity is not synonymous with radiocurability, that the most spectacular rapid melting of tumors with small tissue doses meant, as a rule, rapid recurrence. It became apparent that histological structure, anaplasia and differentiation were not always a guide to prognosis. Glücksmann[10] and Glücksmann and Spear[11] suggested that to estimate the probable response of tissue to radiation, proliferation and differentiation must be considered not as isolated processes but in terms of the quantitative relation of these two processes to one another. From their work resulted the prognostic significance of serial biopsies and an assessment could be made if a given case was likely to be successful or to have an unfavorable course. The cells of the biopsy specimen fall into four categories: dividing, degenerating, resting and differentiating. An unfavorable response of a tumor to irradiation is shown by persistence of mitotic activity, no alteration in the number of resting or degenerating cells and no increase in the differentiating cells; in other words, no qualitative or quantitative alteration before and after irradiation. A favorable response to irradiation is shown by disappearance of mitosis, followed by disappearance of resting cells, and an increase in differentiating and in the degenerating count. It is now ten years since the first case so studied by serial biospies—a cancer of the uterine cervix treated by radium—was correctly forecast to be of good prognosis al-

though clinically a florid and an advanced tumor. It can be summarized that radium was, with roentgen rays, the tool of research by biologists and pathologists and that the knowledge thus acquired played a part in the treatment of tumors.

The question, "Do roentgen rays and radium produce different tissue reactions?" is today as important as it was twenty-three years ago when Ewing[6] in his Caldwell Lecture before the American Roentgen Ray Society (1925) discussed "Tissue Reactions to Radiation" Much technical progress in roentgenologic apparatus, voltage undreamed of then, neutron therapy, the cyclotron, betatron and the multimillion electron volt generators have since then become available and have been used. Can we today say with confidence that therapeutically roentgen radiation is equal in its curative results to that of gamma rays? The progress made in the past twenty years is very substantial but not in all types of tumor. It is obvious that roentgen radiation at one-half to one million volts produces biological effects similar to those of gamma rays. It is also true that in certain groups of neoplastic diseases—Hodgkin's disease, lymphosarcoma, Wilms' tumor and in the treatment of metastasis of many kinds, roentgen rays at 200 to 250 kv. have nearly entirely displaced radium. Yet there is a group of tumors where radium remains the better weapon, where regression of the growth is nearly always predictable and where permanency of results up to twenty and more years has been achieved.

It must be admitted that the use of radium clinically requires a certain amount of surgical skill when interstitial methods are chosen, and that the cooperation of a hospital physicist is essential when surface applicators, plaques or moulds are used; that teleradium requires absolute precision in beam direction, especially when narrow beams are used. All this makes roentgen therapy at the usual 250 kv. a simpler and easier method of treatment. There is also the factor of total tissue dose. I have used 9,000 to 11,000 roentgens to tumors of the tongue before the roentgen was defined and when I was not aware of the dose given. I have continued to give 9,000 to 10,000 r interstitially to the tongue and other lesions with greater precision, accuracy and safety since then. I am not aware that roentgen therapy has achieved such tissue doses, neither am I familiar with statistical proof that epidermoid cancer of mucous membranes can be treated with the same frequency of permanent success by roentgen rays as by radium. The swing of the pendulum from radium to roentgen rays began before World War II. In England it was given a great impetus during the six years of war, when the dangers from bombardment and other difficulties made radium an awkward therapeutic weapon. In some hospitals, nevertheless, teleradium and radium needles continued to be used, albeit with difficulty, practically without interruption. But the swing towards roentgen rays continued. I will remain content by giving a brief review of the treatment by radium of tumors in certain sites and let the achievement speak for itself.

CANCER OF THE UTERUS

No fewer than three Janeway lectures were devoted to Uterine Cancer—that by Henry Schmitz[23] (1938), Wm. P. Healy[12] (1942), and F. W. O'Brien[17] (1947). This in itself goes to show that the American Radium Society has found it a subject worthy of interest. The use of radium in cancer of the cervix is universal, methods have been developed in many countries. Thus we speak of the "Stockholm" method in honor of the pioneer work by Forssell and Heyman at the Radiumhemmet; there is the "Paris" method which differs in dose, timing and technique; there are many modifications, such as the "Manchester" method from the Holt and Christie Institute, the Donaldson-Neary method, where very large quantities of radium are used vaginally. Whatever the variation in technique it resolves itself in the insertion of radium into the uterine canal and the vaginal for-

nices. It has one drawback—the incidence of rectal injuries or burns. In a recent review of 3,392 cases of cancer of the cervix uteri at the Radiumhemmet, there were 313 rectal reactions, or an incidence of 9.2 per cent. Some clinics use roentgen rays as well as radium, mainly to supplement the parametrial dose and the dose to the pelvic wall outside the adequate range of the intracavitary radium. But it remains a supplementary and not the main treatment. What are the results? The most recent and accurate figures (Marie Curie Hospital, London; Holt and Christie Hospital, Manchester) show a *ten year* survival rate of 63 to 65 per cent in Stage I; 34 to 41 per cent in Stage II; 15 to 22 per cent in Stage III; and even in Stage IV, 8 to 4 per cent are obtained. Here is achievement by high ten year survival, by low operative mortality as compared to surgery, by broadening the field of therapy to all stages of the disease. Here is a lesion which is fatal in a mean average in twenty-one months if untreated, curable to the extent of 65 per cent in early cases by radium alone. Can other methods compete with this? There is no doubt room for surgery and room for roentgen irradiation as therapeutic measures, but only exceptionally if the results quoted are to be obtained.

CANCER OF THE TONGUE

I am perhaps more familiar with radium therapy in this site than in any other and I can speak from a personal experience of 365 cases.[3] I would like to postulate that in squamous cell carcinoma of the anterior part of the tongue, that is the tip to the vallecula, radium needles as the sole treatment have proved the most successful therapy and in the posterior or pharyngeal portion (the vallecula) teleradium is the method of choice. At Westminster Hospital, radium has been used for cancer of the tongue since 1924. It is still so used as the first method of treatment and as the only method of treatment in a well defined group of cases. Given a lesion of the tongue, limited to the tongue, radium gives 56 to 60 per cent of five year survival, in cases where the cervical lymph nodes are not involved. Surgery plays an important role in the treatment of operable lymph nodes, when a block dissection is performed. Radium is used if the nodes are deemed inoperable. I think it worth emphasizing that the insertion of needles into a tongue according to well known distribution rules delivers about 9,000 gamma roentgens to the tongue in seven days, that the reaction subsides in a month to five weeks, that in a very large proportion of cases (90 per cent) primary healing occurs, that in about 60 per cent healing is permanent—that is five, ten, fifteen, and twenty years if the patient does not delay seeking advice. Accuracy is essential, in the distribution of the needles, in their radium content, in their retention in situ over the desired period. It is a precise, delicate procedure, which requires planning and skill.

CANCER OF THE UPPER AIR PASSAGES

In discussing the place of radium in the treatment of cancer of the upper air passages, I would like to pay a tribute to Dr. Douglas Quick.[21] In 1937, he delivered the Janeway Lecture on "Carcinoma of the Larynx." His work on cancer of the mouth and upper air passages has been a source of inspiration and encouragement to my colleagues and myself. The present methods which have altered but little in the past five years are mainly teleradium with occasionally supplementary roentgen therapy. In the larnyx itself, the intrinsic group—carcinoma of the vocal cord, the ventricular band, the anterior commissure—offer the most promising cases. Fenestration of the laryngeal cartilage with insertion of needles, as introduced by Finzi and Harmer,[9] has been entirely superseded by teleradium. At Westminster Hospital the technique for laryngeal tumors consists in the use of three fields, left and right laryngeal fields and one anterior field. To overcome the difficulties imposed by the variations in the anatomical configuration of the

neck and by the position and extent of the lesion and to ensure an optimum arrangement for the fields in each individual case, H. T. Flint and C. W. Wilson[24] have constructed suitable frameworks which provide the position of the fields and the direction of the beam. The use of these frameworks permits the placing of the patient within a known field of radiation in preference to providing unknown fields within the patient. With the present unit, it takes four to six weeks to deliver 6,000 r homogeneously to the tissue within the framework of the larynx. At the end of the period of treatment, there is uniform membranous reaction spreading over both cords, the anterior commissure and the arytenoids. The regression of the lesion varies from case to case and with the gross macroscopical types—thus, the papillary growths regress quickly, the ulcerative more slowly. In successful cases 6,000 r is the maximum tissue dose needed and the vocal cords return to a normal appearance. In early cases, that is those considered suitable for laryngofissure limited to one cord, and when the cord is mobile, the appearance within six to eight weeks is indistinguishable from normal and so is the voice. In growths with subglottic extension the results are less spectacular. The advanced and neglected lesions, not suitable for any form of treatment except total laryngectomy, should preferably be treated by surgery, as radiation only exceptionally gives long term results; and much suffering can be inflicted by radiotherapy, be it radium or roentgen rays, in persistence of treatment of advanced and resistant lesions. At the Royal Cancer Hospital, London, M. Lederman, in a series of 40 cases of which 17 were early, obtained five years of freedom of disease in 70 per cent of cases. His series of endolaryngeal cancers between 1933 and 1946 consist of 96 cases treated solely by teleradium and support entirely my personal experience that teleradium, if given skillfully, accurately and in suitable cases, is the method of choice in this site.

Of the extrinsic group, the pyriform fossa carcinoma in men and the postcricoid carcinoma in women form the common groups. Here the results are much worse than in the intrinsic group. But as there is practically no alternative surgical treatment—few cases being suitable for pharyngectomy or laryngopharyngectomy—repeated attempts at improving technique have been made. The method of choice in my clinic is teleradium. Although the results are statistically insignificant, five to twelve year survival has been obtained sporadically in a small number of cases. In these, complete regression of the lesion has been obtained; in the majority of cases palliation only is achieved for two or three years. The problem is still unsolved.

NEOPLASMS OF THE MAXILLARY ANTRUM

In this situation, radiotherapy has completely altered the prognosis. I will deal in this contribution with the treatment of carcinoma of the antrum. Sarcoma of the antrum, rare and radiosensitive, is equally well cared for by roentgen irradiation. But in the carcinoma group a combination of surgery with radium therapy has proved a valuable method. It is based on the approach devised by Öhngren[18] and consists in the transpalatal access to the tumor, the removal of the hard palate and the destruction of the growth by diathermy; this is followed by intracavitary application of radium on a prosthetic appliance made for each individual patient. The dosage rate aimed at varies from 50 to 70 gamma roentgens per hour, and ten to twelve hours' treatment daily is given. A total of 8,000 gamma roentgens is aimed at. The advantages of this method can be summarized as follows: (1) it gives access to the tumor without any external mutilation; (2) it provides drainage of the maxillary antrum, the ethmoidal cells and, if necessary, the sphenoidal sinuses; (4) following irradiation there remains an inspection window and so recurrences can be seen at the earliest stage. Speech is restored by a dental plate carrying an obturator. My oldest patient,

now eighty-six years of age, has survived free from disease for twenty-two years following this treatment. In all, a small personal series of 55 cases so treated has yielded just over 50 per cent of survival with freedom of disease for five years upwards.[4] Many modifications of the method described are applicable; thus preoperative irradiation in all or partly, can be given by teleradium; or both preoperative and postoperative irradiation can be used. The surgical principle, however, is the same—transpalatal approach and the use of the diathermy, and radiotherapy is by intracavitary radium or by teleradium.

CARCINOMA OF THE BLADDER

Carcinoma of the bladder is a transitional cell carcinoma. Its three clinical varieties—papillary, ulcerative and nodular—are of similar histopathological type. The radiosensitivity of these growths is low, and a considerable tissue dose is needed to produce regression of the lesion. Of the main forms of radiation therapy—radium and roentgen rays—radium is to date undoubtedly the more efficacious. Roentgen irradiation as the sole method of treatment has, in my experience, failed to produce regression; a study of the literature supports this view. The main reason, I believe, is the difficulty to deliver to the tumor in the bladder a dose of roentgen radiation adequate to control the growth, although hemorrhage may be arrested or controlled. This fact is recognized and attempts have been made to raise the daily dose to 300 r or more, to use as many as six ports of entry, to push the treatment to the limit of skin tolerance, namely blistering. But these gallant attempts have not resulted in any great improvement, at least with the use of 200-250 kv. There are, however, indications that with higher voltage—1,000 to 2,000 kv.—and with improvements of both apparatus and technique, the position may change.

With radium the problem of adequate dosage can be solved by the use of interstitial radiation. In selecting the method of treatment the important questions are: What type of lesion is suitable for radium therapy? What is the technique of choice? What is the optimum total dose and dosage rate? The type suitable for radium therapy is a lesion of moderate size, located at the base or lower part of the bladder, of the infiltrating or ulcerative type. Small growth on the roof or sides, accessible growths of moderate extent can be dealt with by partial cystectomy; extensive lesions where complete regression by irradiation cannot be confidently anticipated should be considered for total cystectomy if the patient is fit and willing to undergo this ordeal. The papillary growths, if obviously malignant and still operable, are dealt with by a combination of diathermy and radium. If these criteria are applied, about one-third of all cases of carcinoma of the bladder are found to be suitable for radium.

As regards technique, the endoscopic method, that is, the introduction of radon seeds through a cystoscope, has naturally attracted the attention of urologists. It is suitable in early cases of localized growth in the absence of infection. Only a very few cases fulfill these desiderata.

The advantages of the endoscopic methods are outweighed by the following disadvantages: (1) The wall thickness of the seed is limited by the bore of the instrument; this means that the screenage is limited to 0.3 mm. of platinum; severe reactions follow and risk of infection is increased. (2) The distribution of small radium foci in regular geometrical pattern is difficult, with the result that, except in very small lesions, some areas are overirradiated, while others receive a sublethal dose. (3) The falling intensity of radon mitigates against the delivery of the necessary total dose without considerable risk of necrosis.

The technique of choice is accurate needling under direct vision through a wide suprapubic cystotomy. Suitable retractors, adequate exposure, good illumination provide the necessary access to the growth. A choice of needles of various lengths, but

of similar linear intensity, must be available; screenage should be preferably 0.8 mm. of platinum. The actual distribution of the needles depends upon the anatomical configuration of the lesion; most growths can be adequately treated by a single plane implant; patterns previously prepared for different lesions are used. The total dose aimed at is high, namely 7,000 to 8,000 gamma roentgens. It can be achieved without inflicting burns if the dosage rate is about 35 to 45 gamma roentgens per hour; with such low intensities the total time of irradiation is about nine to ten days. The amount of radium required is small and varies according to the volume of tissue to be treated and its surface extent. The needles must be placed accurately in position and steps taken to ensure that they stay in position. An area of at least 1.5 cm. of apparently normal bladder should be irradiated beyond the periphery of the lesion. Like all surgical procedures, the needling of the bladder requires care, skill and patience; it also requires training and practice. But, above all, it is not a treatment which can be carried out unless special facilities are available in specially equipped institutions. The closest cooperation between urologist, radiotherapist and physicist is a sine qua non. It is this absence of cooperation which has given needling of the urinary bladder rather a sinister reputation associated in the minds of many with burns, cystitis, urgency, frequency, uncontrollable pain resulting is miseries compared with which the natural distress of cancer of the bladder pales into insignificance. I emphasize this point, as it is essential not to gloss over the difficulties or the dangers of the method. Results, however, have justified this treatment and apparently total regressions up to a period of ten years have been achieved. The treatment of cancer of the bladder by radium is as much a surgical procedure as diathermy or excision—it should enlarge and not diminish the urologist's field of usefullness.

CANCER OF THE SKIN

I will say little of the benefits of radium in the treatment of cancer of the skin, as this is well known and still holds its place equally with roentgen rays. I will content myself with the mention of one skin lesion, epithelioma of the penis. In this site, early cases treated by needling regress with little mutilation and no undesirable side effects. Advanced and extensive lesions, involving the urethra, the corpora cavernosa or the corpus spongiosum are not suitable for radium; in such cases surgery must be resorted to in spite of the grave mutilation it inflicts. In early cases, needling with radium has achieved freedom of recurrence up to eighteen years.

CANCER OF THE BREAST

As a palliative measure for recurrences or in the treatment of inoperable cases, radium has long been in use. Geoffrey Keynes,[15,16] however, was the first to treat operable and early cases by radium as an alternative to radical amputation. Radium therapy in breast cancer has been superseded by roentgen therapy, but it played an important part in the development of radiation therapy in this site. Needling of the breast, either alone or in association with surface plaques, has given complete regression of the disease and survival rates very nearly equal to those of surgery in some cases. Radiation is of key importance in the treatment of advanced cases and as a preoperative measure. There can be no doubt that the prognosis in cancer of the breast can be materially improved by the judicious, careful and expert use of radiation either as the sole method of treatment or in combination with surgery. Early diagnosis remains the greatest single factor influencing prognosis. Preoperative and postoperative irradiation, preferably with roentgen rays, but in selected cases with radium, has not only improved end results, but rendered a larger proportion of patients amenable to treatment.

Successful radiotherapy of cancer depends primarily on a knowledge of the disease, its natural history, its mode of spread, its response to various methods of treatment and to various techniques of irradiation. Radiation is not a panacea for all cancer cases and should not be used to the exclusion of surgery, unless it is better than surgery. Similarly, radium should not be used to the exclusion of roentgen rays, or roentgen rays to the exclusion of radium; both methods have their advantages in certain sites; they are often complementary. If the benefits of treatment are to be obtained to the fullest measure, it is important to recognize the limitations of each method. No radiotherapy department can be adequate without facilities for both radium and roentgen therapy and a specialist trained in the use of both, and eager to use all methods. No cancer clinic can rely upon radiation alone, and surgery as well as chemotherapy has its very important place. It must unfortunately be recognized that quite apart from research purposes, the choice of the method of treatment is often dictated by the facilities available, by bias of the clinician to a certain given method of treatment and by prejudice against other methods. What is the achievement of radium? It is the therapeutic measure of choice in cancer of the uterine cervix, in cancer of the lip, tongue and mouth, in cancer of the larynx and the antrum, and the urinary bladder—all accessible tumors of moderate topographical extent, and medium grade of radiosensitivity. Radium is equal in efficacy and often more certain than roentgen radiation in cancer of the skin, including the penis and the anal canal. In highly radiosensitive tumors, lymphosarcoma, lymphadenoma, plasmocytoma, roentgen therapy should be preferred. In tumors of bone and in cancer of the breast, roentgen rays are preferable on the grounds of simplicity. In deep-seated and inaccessible tumors, technical difficulties preclude the use of radium.

In looking back on a quarter of a century of work with radium in the treatment of cancer, it seems clear that for its use, surgical as well as radiological training is of great importance and that lack of surgical ability limits the use of radium to external methods of treatment and these are more easy of accomplishment by roentgen rays. My impression is that apart from total dose and dosage rate, the biological effects of radium and roentgen rays, although similar, are not identical and this profoundly affects the long term results of treatment in most sites.

This review of the Achievement of Radium in the Fight against Cancer is based on the work done in the great clinics in the United States and in Europe—of these, three institutions fill the center of the stage —the Memorial Hospital, New York, the Radium Institute of Paris, and the Radiumhemmet in Stockholm. My own field of activity, the Westminster Hospital in London, has, in company with all other London teaching hospitals, passed through the war years with added difficulties. You may be interested to know that when the bombs were dropping fast, there was unveiled in 1943, in one of the radiotherapy wards of the Westminster Hospital, a tablet commemorating the fact that American citizens were supporting in that ward, beds for patients from London air-raid shelters. There is this added link which humanity has forged between us and this is an opportunity of bringing back our warmest appreciation which the passing of five years has mellowed, but not dimmed.

The achievement of radium can be counted in the years added to the lives of countless numbers of patients; this could be assessed statistically, but it is not possible to compute in figures, the relief of pain, palliation and temporary arrest of disease and prolongation of life which has been achieved in addition. The advances made in pure science cannot yet be fully understood. If my review of these achieve-

ments is incomplete and has many gaps, may I plead Hippocrates' first aphorism that "Life is short and the Art long; the Occasion fleeting; experience fallacious and judgement difficult."

Westminster Hospital
London, England

REFERENCES

1. Bergonié, and Tribondeau, L. Premieres experiences sur le rat blanc. *Compt. rend. Soc. de biol.*, 1904, *57*, 400; 592; 595.
2. Bohn, G. L'influence du radium sur les animaux en voie de croissance. *Compt. rend. Acad. d. sc.*, 1903, *136*, 1012.
3. Cade, S. Discussion on the treatment of cancer of the tongue. *Proc. Roy. Soc. Med.*, 1947, *40*, 409.
4. Cade, S. Malignant Disease and its Treatment by Radium. Second edition. Vol. II. John Wright, Bristol, 1948.
5. Dominici, H. Modifications histologiques déterminées par le rayonnement du radium. *Arch. d'élect. méd.*, 1907, *15*, 835.
6. Ewing, J. Tissue reactions to radiation. Am. J. Roentgenol. & Rad. Therapy, 1926, *15*, 93–115.
7. Ewing, J. Early experiences in radiation therapy; Janeway Memorial Lecture, 1933. Am. J. Roentgenol. & Rad. Therapy, 1934, *31*, 153–163.
8. Failla, G. Some aspects of the biological action of ionizing radiations; Janeway Lecture, 1939. Am. J. Roentgenol. & Rad. Therapy, 1940, *44*, 649–664.
9. Finzi, N. S., and Harmer, D. Radium treatment of intrinsic carcinoma of the larynx. *Brit. M. J.*, 1928, *2*, 886–889.
10. Glücksmann, A. Preliminary observations on the quantitative examination of human biopsy material taken from irradiated carcinomata. *Brit. J. Radiol.*, 1941, *14*, 187–198.
11. Glücksmann, A., and Spear, F. G. The qualitative and quantitative histological examination of biopsy material from patients treated by radiation for carcinoma of the cervix uteri. *Brit. J. Radiol.*, 1945, *18*, 313–322.
12. Healy, W. P. The role of the gynecologist in the field of cancer; Janeway Lecture, 1942. Am. J. Roentgenol. & Rad. Therapy, 1943, *49*, 1–10.
13. Janeway, H. H. The relation of gastrostomy to inoperable carcinoma of the esophagus with a description of a new method of performing gastrostomy. *J.A.M.A.*, 1913, *61*, 93–95.
14. Janeway, H. H. Radium Report of the Memorial Hospital, New York. Second series, 1923. Paul B. Hoeber, New York, 1924.
15. Keynes, G. Radium treatment of primary carcinoma of the breast. *Lancet*, 1928, *2*, 108–111.
16. Keynes, G. Hunterian lecture on radium treatment of carcinoma of the breast. *Lancet*, 1930, *1*, 439–442.
17. O'Brien, F. W. The radium treatment of cancer of the cervix; a historical review; Janeway Memorial Lecture, 1946. Am. J. Roentgenol. & Rad. Therapy, 1947, *57*, 281–297.
18. Öhngren, L. G. Malignant tumours of the maxillo-ethmoidal region. *Acta oto-laryng.*, 1933, supp. 19, pp. 1–476.
19. Perthes, G. Versuche über den Einfluss der Röntgenstrahlen und Radiumstrahlen auf die Zellteilung. *Deutche med. Wchnschr.*, 1904, 632–668.
20. Price-Jones, C., and Mcttram, J. C. Contribution to the study of in vitro plasma cultures of mouse carcinoma and rat sarcoma. *Arch. Middlesex Hosp.*, 1914, *33*, 21.
21. Quick, D. Carcinoma of the larynx; Janeway Memorial Lecture, 1937. Am. J. Roentgenol. & Rad. Therapy, 1937, *38*, 821–853.
22. Quimby, E. H. The specification of dosage in radium therapy; Janeway Lecture, 1940. Am. J. Roentgenol. & Rad. Therapy, 1941, *45*, 1–17.
23. Schmitz, H. The development of the forms of treatment in carcinoma of the uterine cervix during the last one hundred years; Janeway Memorial Lecture, 1938. Am. J. Roentgenol. & Rad. Therapy, 1938, *40*, 805–816.
24. Wilson, C. W. Radium Therapy; Its Physical Aspects. Chapman and Hall, Ltd., London, 1945.

A. N. ARNESON

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A CONCEPT OF THE CLINICAL USE OF RADIUM*†

By A. N. ARNESON, M.D.
ST. LOUIS, MISSOURI

THE Thirtieth Annual Meeting of the American Radium Society occurs in a year of considerable historical significance. Nineteen hundred and forty-eight marks the Fiftieth Anniversary of the discovery of radium. It is appropriate that we take cognizance of that event. In planning a celebration commensurate with the occasion, a number of modifications have been made in the usual order of scientific and social affairs of the Society.

It is our good fortune to have several distinguished guests from overseas. Participation of those visitors in the scientific sessions elevates the program to an international level not attained before. Such an exchange of knowledge and experience is well timed after the lack of assembly incurred during the War years. The discussions to be undertaken will include problems to be met in further advance in radiation treatment. At one point on the program one of our members well suited to the task will pay tribute to the discoverers of radium, and elaborate upon the fascinating history of the development of radioactivity. We are apt to forget the profound impressions that fell upon early pioneers in the clinical use of radium. The degree of palliation obtained in patients with hopeless prognoses must have been in sharp contrast to that which was to be expected for any other method then in use. The relative simplicity of treatment in more favorable cases must have been in sharp contrast to the hazards of radical surgery. It is not surprising that tremendous enthusiasm was developed.

In this day and time we find radium occupying a somewhat different position in clinical practice. Methods of treatment have advanced beyond the stage of empiricism gained from experience by trial and error. Technical advances have resulted in the development of a number of different methods for administering electromagnetic or particulate radiations. The multiplicity of methods that can be used for irradiating tissue has lessened the preëminence of radium in clinical practice. Other factors have mitigated against interest in radium as a method of treatment. Advance in knowledge of medicine has extended the applicability of surgery. Some clinical departments have set out to explore again the use of certain operative procedures that had been more or less discarded. Any challenge that one method of treatment presents another is wholesome criticism that should result in improvement in clinical care. The researches in surgery have sometimes been interpreted, however, as trends in treatment. The impression is gained that the use of radium is decreasing. As a result, many inadequate operations are performed in pursuit of what is believed to be an established modification in clinical practice. Extension of that attitude will result in neglect of clinical study and clinical teaching, with recession in knowledge of the clinical use of radium in conditions for which it is indispensable. Radium may be replaceable by certain of the newer isotopes, but there is no foreseeable time at which gamma-ray emitters will not be essential for the focal intensities of irradiation required in the treatment of certain types of lesions.

Of the several technical developments that may have acted to replace radium as a method for irradiating patients, the most important has been the use of roentgen rays. Whatever that effect may have been, it would be expected to have occurred during the past twenty-five years. Begin-

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† From the Edward Mallinckrodt Institute of Radiology, the Department of Obstetrics and Gynecology, and the Barnard Free Skin and Cancer Hospital, Washington University School of Medicine, St. Louis, Missouri.

ning with 1922, spot surveys were made from the operating room record of the Barnes Hospital for every fifth year to 1947. For each of those years the number of radium treatments was determined as well as the number of patients treated. The number of radium treatments has increased at a somewhat greater rate than the number of patients. Those data were then correlated with statistics available upon total hospital admissions, excluding obstetric and pediatric patients. The increase in patients treated with radium has followed closely the increase in total hospital admissions. The ratio of radium patients to total admissions for 1932 is 1:56. For 1942, the value is 1:56, and in 1947, it is 1:55. There has, therefore, been no decrease in the use of radium at the hospital in question. Of the total number of radium treatments for the specified years, 57 per cent were applied for gynecological lesions.

TABLE I

STATISTICAL DATA FROM THE OPERATING ROOM RECORD OF THE BARNES HOSPITAL GIVING THE NUMBER OF RADIUM TREATMENTS FOR SPECIFIED YEARS. THE RATIO OF PATIENTS TREATED WITH RADIUM TO TOTAL HOSPITAL ADMISSIONS (EXCLUDING OBSTETRIC AND PEDIATRIC PATIENTS) IS SHOWN FOR CERTAIN YEARS

	Year					
	1922	1927	1932	1937	1942	1947
Radium patients	55	65	105	155	193	315
Radium treatments	57	66	110	170	208	361
Total hospital admissions			5,923		10,882	17,256
Ratio radium patients to total admissions			1:56		1:56	1:55

It is difficult to arrive at an accurate estimate of volume of radium work done each year in the United States. The May 1, 1948, issue of the *Journal of the American Medical Association* presents a list of 336 hospitals approved for training in radiology. The number of radium treatments performed annually is given for all but 81 of the named institutions. It can be assumed that data are incomplete for some hospitals not reporting radium treatments, and in others approval for training may have been granted on the basis that experience in radium treatment is gained by access of radiological residents and fellows to other affiliated clinical services or institutions. Hospitals approved for training in roentgenology or diagnostic roentgenology alone would not be expected to show a sizable number of radium treatments, but of the 235 designated for training in radiology or therapeutic radiology, 122 report fewer than 100 treatments per year. That indicates that radium is used more than twice a week in only 113 American hospitals. The number of treatments exceeds 300, about one per working day, in only 21 of those institutions. Four hospitals report more than 1,000 treatments, and the greatest single number is 4,227. The majority of radium work appears to be concentrated in about 6 per cent of the approved institutions. If the statistics here given are reasonably correct, then the number of institutions with a flow of clinical material adequate for sound teaching are limited in number. That is not intended to imply that quantity is an index of quality, but it is obvious that effective training depends in part upon experience gained by repetition.

Data given in a list of hospitals approved for radiological training are not intended to present a complete summary of radium work in the United States. There are several prominent members of this Society, for example, who perform radium treatments at institutions not set up for resident

and fellowship training. Furthermore, many patients are treated on an ambulatory status. It is unfortunate that probably most of that valuable material is lost for teaching purposes.

The clinical use of radium is distributed among dermatologists, gynecologists, radiologists, surgeons, and many others. There is in this country no standard qualification required of an individual employing radium in clinical practice. The absence of restriction upon ownership, rental, and sub-rental of radium makes the material available to all who find indication for its use. Lack of organization for administering the clinical use of radium is to a large extent responsible for the empirical procedures followed so frequently. It is probable that quality of radiation treatment varies more widely than does perfection of surgical technique and judgment. In the attempt to improve quality of work, it is not an uncommon practice for surgical divisions to require consultation, in specified circumstances, before performance of certain operations. Consultation upon use of radium is usually made only upon a voluntary basis, and in many instances in which advice is sought, the consultant gives an opinion expressed in terms of milligram-hours, without examination of the patient. Specification of a required treatment in total milligram-hours is no more precise than to state that a patient with a tumor mass requires a certain number of minutes of surgery.

It is obvious that one of the weak points in the system is the method of teaching. The time and effort required for adequate training in radiation therapy is as formidable as that needed for perfection in any of the surgical specialties. Basic knowledge must not only include anatomy, pathology, and physics of radiation, but also clinical diagnosis, biologic effects of radiation, and the natural history of tumors. Broad training of that scope is rarely provided in a single institution. It can scarcely be presented in a general radiological department in which the resident or fellow divides his time between roentgen diagnosis and radiation treatment. Neither is it likely to be supplied in any of the affiliated clinical departments employing radium. Adequate teaching material is to be found only in the larger centers. Adequate facilities for teaching might be attained in an autonomous department for radiation treatment. Graduates from such departments would elevate the standard of treatment procedures. The disappointing effects of too much or too little irradiation would be lessened. Exposure to disputes or changing trends in methods of treatment would be reduced. A more orderly advance in treatment of cancer would be attained.

Improvement in the use of radium cannot be separated from the general problems in radiation treatment. Attainment of a standard of teaching at the level in question necessitates centralization of clinical material and facilities as well as personnel in clinical medicine and the related sciences. Evidence that centralization of that order is going forward is indicated by the fact that large radium services are found in fewer than 10 per cent of American hospitals approved for radiological training. The point might well be made that the scope of radiation treatment is too broad for one individual. The same problem has been responsible for segregation of surgical specialties into limited anatomical fields. In the larger centers the processes of evolution might very well result in specialization into different anatomical divisions within the department of radiation treatment. In such departments it is not unreasonable to expect in some of the now recognized specialties the development of individuals engaged in the treatment of cancer by radiation or by surgery. The point of emphasis should be placed upon the importance of elevating the radiation therapist to the recognition that his specialty deserves. Active demonstration of the complexities of radiation treatment by performance of a high standard of precision instead of present empirical methods would bring realization of the hazards involved to other

members of the medical profession. That can best be done by elevating the standard of teaching. Mechanisms for controlling the administration of radium would then be less important. Fulfillment of those aims will advance and preserve our system of medicine. It is not to be implied that the centralization necessary for teaching is equally essential for patient care. With reasonable saturation of the need for highly qualified radiation therapists, clinical practice could be decentralized to a degree similar to that which is attained in the major surgical specialties.

Prerogative for expressing the aims here given is taken in the presentation of a presidential address. Certification of qualifications falls within the sphere of the various Specialty Boards. Standardization of minimal requirements for teaching the clinical use of radium will provide Specialty Boards with a uniform basis for establishing a suitable scheme of certification. Within the Society are the individuals most capable of providing the teaching and training required for modification of our present system. A study of the problems at hand should be one of the projects of the American Radium Society.

4952 Maryland Ave.
St. Louis 8, Mo.

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EFFECTIVE DOSAGE LEVELS IN INTERSTITIAL RADIUM THERAPY

By BENJAMIN JOLLES, M.D., D.M.R.
Radiotherapy Department, General Hospital
NORTHAMPTON, ENGLAND

THE early empirical techniques in radium therapy of malignant conditions were found to give good results in a number of cases. Quite often, however, the persistence or recurrence of growth and the appearance of necrosis showed only too well that faults of technique existed. Even in the best hands mishaps occurred which were not entirely due to the nature of the lesions dealt with.

In the past decade the empirical methods have been superseded. Dosage systems were devised whereby specific arrangements of radioactive foci are used in such a way that the dosage is known and controlled from beginning of treatment. The dosage system of Paterson and Parker (Paterson and Parker[1] 1934, Paterson, Parker and Spiers[2] 1936, Paterson and Parker[3] 1938) has proved to be sound, from both clinical and physical points of view, and is now adopted in most radiotherapy institutions.

By obeying the rules of their dosage system, irradiation at a uniform average level throughout the treated volume of tissues is achieved. It might be stressed, however, that there are finer details of implantation which obviously cannot be put in the form of rules as they apply to individual cases, in which experience teaches one how and where an "empirically" placed needle can make all the difference in obtaining the best result, and where the strict application of the rules is not feasible on anatomical or clinical grounds.

The distribution rules and charts in Paterson and Parker's dosage system answer two cardinal points which interest the practical radium therapist, i.e., how much radium is required and how it should be arranged in any particular case.

One of the outstanding problems facing the radiotherapist is that of the dosage levels, and the tumor "lethal" dose in the region of 6,000 r over a period of seven days, as suggested by Paterson, is a guide which has to be supplemented by experience and often by flair.

In this paper the problem of the amount of radiation to be delivered is discussed and an approach on novel lines postulated, and suggestions made which might be found helpful as a supplement to the Paterson and Parker dosage system.

According to the size of the implant the dose required for a given biological result varies and as suggested by Paterson in the biological section of his paper, 5,500 r to 7,000 r have to be given. In the assessment of the dose required only the volume of tissues to be treated is taken into account in the dosage system.

It is undeniable that the destruction of cells in the tumor area by ionizing radiations is not the whole story of the chain of events leading to the resolution and disappearance of the growth, and that many other concomitant factors come into play. Of these, the intrinsic resistance of normal tissues to malignant growth is worth remembering, and, although it is fair to assume that the organic barriers of resistance have been overcome at the time and site of appearance of the growth, a residual force undoubtedly remains and plays an important role in checking the growth. This local resistance comes more to the forefront when the balance of forces is upset by the effect of radiations.

It seems therefore necessary to take into consideration the area and volume of surrounding normal neighboring tissues which exert an influence on the behavior of the tumor. This amount of normal tissues through which nutritional fluids pass into the tumor territory and through which

toxic demolition products flow from the irradiated volume of tissues is of great importance. These tissues bear the brunt of radiation injury and contribute to repair. Taking into account not only the volume of tissues irradiated, that is, its size, but also its shape and the volume of the neighboring tissues, a rather more complete set of data is available for the assessment of dosage levels to be delivered.

In previous work[4] (Jolles, 1941) it was found that in animal experiments, the

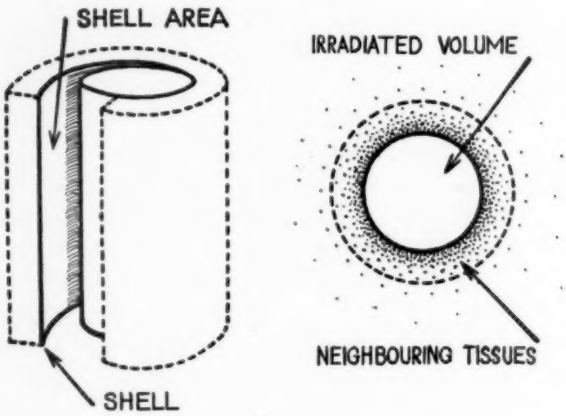

FIG. 1.

severity of skin reaction due to roentgen rays depends upon the size of the area irradiated, and by means of various devices (grid, sieve, anulus, etc.), it was shown that, the dose per unit area remaining unchanged, the reaction becomes a minimum when the adjacent normal tissues can exert their maximum protective role.

I have shown that:

(a) When small areas of skin (up to 3 cm. in diameter) are irradiated, the dose required to produce a given degree of skin reaction increases as the size of the field diminishes. Thus the degree of effect depends on the product dose-in-roentgens times area rather than on dose alone.

(b) If an area is irradiated through a sieve, the reaction produced is approximately the same as would be produced if the whole area were given a much smaller dose. Thus when a sieve was used, having 11 per cent of its area transparent, and 89 per cent opaque, the skin reaction produced was about what would be expected with a ten times smaller dose spread over the whole area.

Subsequently an attempt has been made to co-ordinate data obtained from clinical observations for the tolerance dose levels in deep roentgen therapy.

Working on the theory, based also on clinical experience, that the skin tolerance dose in deep roentgen treatment depends not only on the size, but also on the shape of the field, an empirical formula has been evolved enabling the optimal tolerance doses to be assessed under any condition of treatment. This has been arrived at by trial and error, the formula being amended from time to time according to clinical observations. The factor controlling the effect of the field was $\sqrt[3]{p/a}$ where p is the perimeter of the field and a the area (Jolles[5] 1946, Jolles and Mitchell[7] 1947).

Now considering a cross section of tissue of finite thickness in the path of a roentgen-ray beam, it is seen that the ratio p/a is also the ratio between the surface of the surrounding untreated tissue and the volume of the section. This suggested that the theory might be adapted to irradiation of blocks of tissue by radium (Jolles[6] 1946). In such cases the whole perimeter or shell surrounding the treated volume must be taken into account, so that the ratio $\sqrt[3]{\text{Shell/Vol.}}$ would be analogous to the ratio $\sqrt[3]{p/a}$ in the deep roentgen therapy case.

Knowing from clinical experience that a dose of 6,000 r delivered over a period of one week providing that the rules of distribution of the Paterson and Parker system are strictly obeyed, is adequate for a volume of about 75 cc., the relative effective dose levels for volumes of different sizes can be calculated. In Table 1 dose levels for cylinders of different sizes are presented, and although several of these are tentative ones, it appears within reasonable certainty that the doses suggested are the correct ones.

It is difficult to decide about the thickness of the shell of neighboring tissues

around the irradiated block that has to be computed, and therefore the area of the shell has been taken into consideration. This appears sufficiently accurate in cylindrical implant calculations with the following provisions:

(1) When one end of the implanted volume of tissues is on the surface of body or organ (skin, dorsum of tongue, etc.) or adjacent to a region from which no contribution to repair can be expected (mandible, terminal implants or moulds, i.e., in penis or fingers) the shell area to be computed is smaller and therefore the tolerance dose is correspondingly smaller.

(2) When one end of the implanted volume or plane is uncrossed by needles the values of the relative tolerance doses remain unaltered.

(3) Two plane implants with a separation greater than 1.5 cm. are treated as cubic volumes. A slab of tissue 0.5 cm. thick outside the radium needles in the planes should be included in the assessed volume.

Figures 2*A* and *B* are anteroposterior and lateral roentgenograms showing position of needles, with ring over lips, used for calculation of magnification factor. "George R." Ulcerated infiltrating squamous carcinoma of inferior aspect of tongue, with infiltration of floor of mouth. In this case an attempt was made to cross also the bottom end of the volume. However, only the anterior part of the tumor received an appreciable contribution from these "cross" needles.

Table I

RELATIVE EFFECTIVE DOSAGE LEVELS FOR CYLINDRICAL IMPLANTS

Diameter cm.	Height cm.	Vol. cc.	Shell Area		Shell/Volume		$\sqrt[3]{S/V}$		Relative Doses	Relative Doses
			Total	One End Neglected						
			(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)
2	2	6.28	18.84	15.7	3.0	2.5	1.44	1.35	8000 r	7700 r
	4	12.56	31.4	28.26	2.5	2.25	1.35	1.305	7400	7450
	6	18.84	43.96	40.82	2.34	2.17	1.325	1.29	7200	7400
	10	31.4	69.08	65.94	2.2	2.1	1.3	1.273	7100	7270
3	2	14.2	33.0	25.94	2.33	1.83	1.32	1.22	7200 r	6950 r
	4	28.4	51.9	44.8	1.83	1.58	1.22	1.16	6650	6625
	6	42.6	70.7	63.6	1.66	1.49	1.18	1.138	6450	6500
	10	71.0	108.4	101.3	1.53	1.43	1.15	1.12	6300	6400
4	2	25.1	50.2	37.66	2.0	1.5	1.26	1.14	6900 r	6500 r
	4	50.2	75.3	62.76	1.5	1.25	1.14	1.07	6250	6100
	6	75.3	100.4	87.86	1.33	1.17	1.1	1.05	6000	6000
	10	125.6	150.8	138.2	1.2	1.1	1.06	1.03	5800	5900
5	2	39.2	70.6	51.0	1.8	1.3	1.21	1.09	6600 r	6250 r
	4	78.4	102.0	82.4	1.30	1.05	1.09	1.013	5950	5800
	6	117.6	133.4	113.8	1.13	0.97	1.04	0.985	5650	5620
	10	196.0	196.2	176.6	1.0	0.90	1.0	0.965	5500	5500

"Volume" implant. Irradiated volume 55.5 cc. Shell area 62.8 sq. cm., $S/V = 1.13$. $\sqrt[3]{S/V} = 1.04$. Effective tolerance dose = 6,240 r.

Figures 3*A* and *B* are anteroposterior and lateral roentgenograms showing position of needles. One end uncrossed. "Henry D." Ulcerated growth on inferior aspect of tongue and floor of mouth, which is infil-

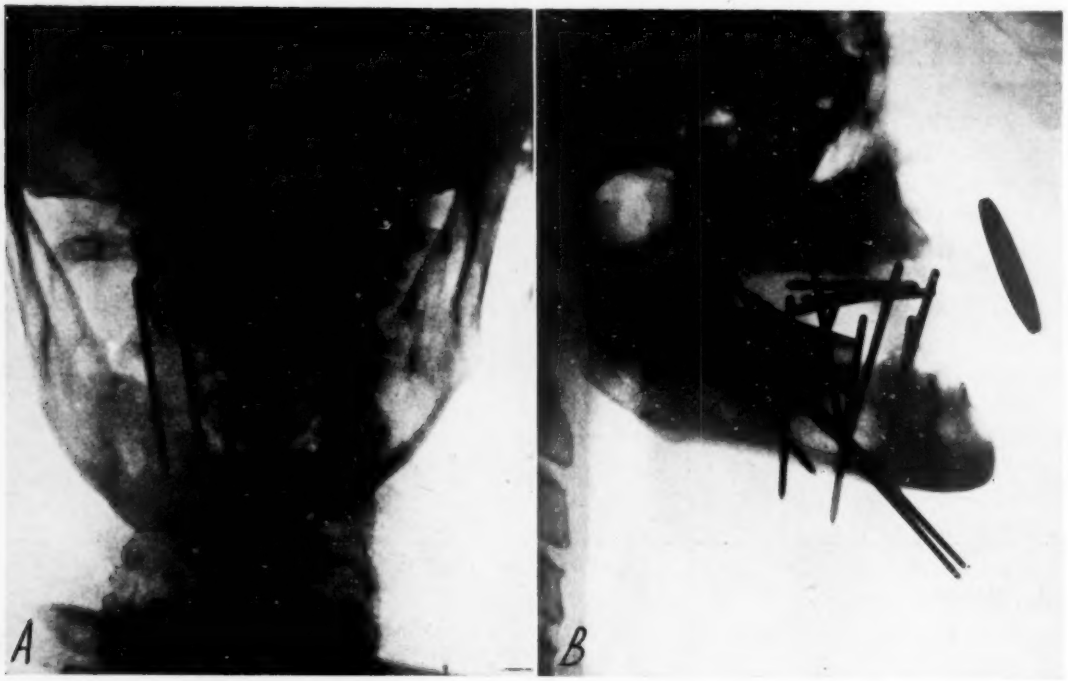

FIG. 2. *A*, shows correct position of needles. The two needles crossing the lower end of the cylinder do not reach the posterior parts of the treated volume but their contribution to the tumor area is not negligible in this case. *B*, the ring (*R*) on the lips of the patient is used for calculation of the magnification of the needles for irradiated volume assessment.

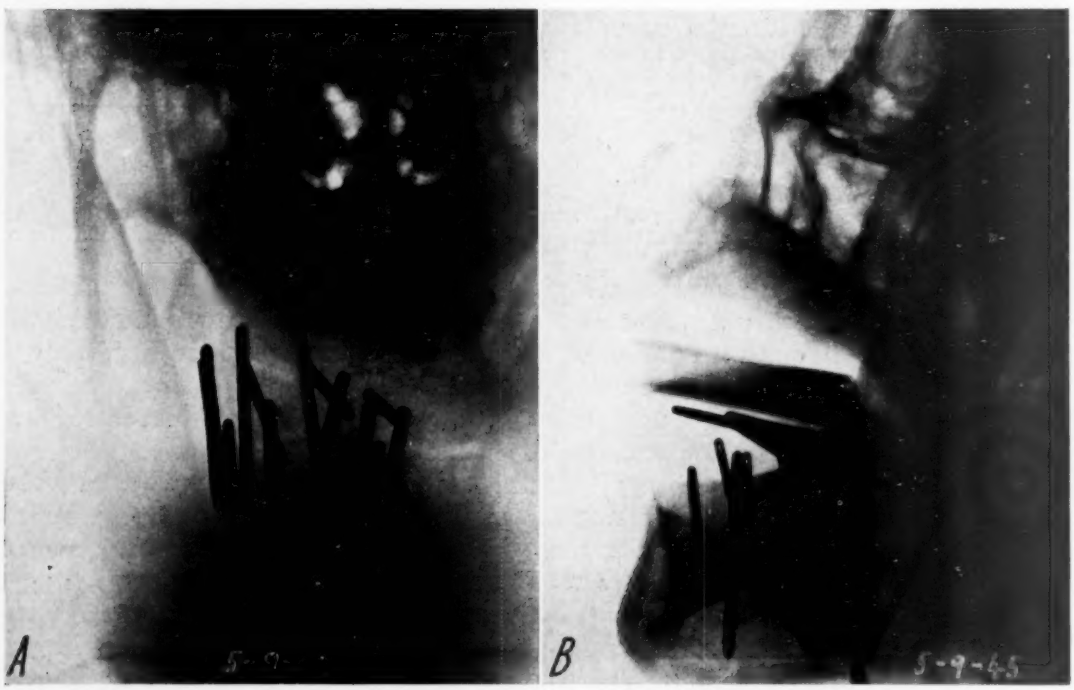

FIG. 3, *A* and *B*.

trated almost to the alveolus, but without bone involvement.

"Volume" implant. Irradiated volume 50.0 cc. Shell area 62.5 sq. cm. $S/V = 1.25$. $\sqrt[3]{S/V} = 1.07$. Effective tolerance dose = 6,400 r.

The aim of destroying malignant growth by means of high doses of roentgen or gamma rays has led in recent years to an increase of dosages, and the time has now been reached when a reconsideration of tolerance dose levels is overdue. Both experiment (genetics) and clinical findings show that there are many concomitant physiological factors which come into play in the treatment of tumors besides the direct effect of roentgen or gamma rays on malignant cells. It is therefore reasonable to assume that the maximum permissible dosages are not necessarily the best ones, even if these fall short of early or late necrosis (Ellis[8] 1942, Windeyer[9] 1942, Koller and Smithers 1946).

In the described method of dose assessment an attempt is made to conciliate two seemingly opposing views:

(a) The delivery of an effective and adequately high dose of radiation.

(b) The preservation of the connective tissue structures which contribute to repair and recovery.

Although in interstitial therapy one can hardly be up to the accuracy implied in this article and tables, yet the attempt to account for the area surrounding the implanted volume seems worth while, as these represent the unknown factors exercising an influence on the treated volume of tissues.

SUMMARY

A quantitative method of assessing effective tolerance dose levels in interstitial radiotherapy of malignant growths is described.

The importance of the perimeter/area ratio in deep roentgen treatments and of the shell/volume ratio in radium therapy is stressed.

General Hospital
Northampton, England

REFERENCES

1. Paterson, R., and Parker, H. M. Dosage system for gamma ray therapy. *Brit. J. Radiol.*, 1934, *7*, 592–632.
2. Paterson, R., Parker, H. M., and Spiers, F. W. System of dosage for cylindrical distributions of radium. *Brit. J. Radiol.*, 1936, *9*, 487–508.
3. Paterson, R., and Parker, H. M. Dosage system for interstitial radium therapy. *Brit. J. Radiol.*, 1938, *11*, 252–266.
4. Jolles, B. X-ray skin reactions and protective role of normal tissues. *Brit. J. Radiol.*, 1941, *14*, 110–112.
5. Jolles, B. Dose control in radiotherapy. *Nature*, London, 1946, *157*, 552.
6. Jolles, B. *Brit. J. Radiol.*, 1946, *19*, 143.
7. Jolles, B., and Mitchell, R. G. Optimum skin tolerance dose levels. *Brit. J. Radiol.*, 1947, *20*, 405.
8. Ellis, F. Tolerance dosage in radiotherapy with 200 kv x rays. *Brit. J. Radiol.*, 1942, *15*, 348–350.
9. Windeyer, B. W. *Tr. Faculty Radiol.*, March, 1942.
10. Koller, P. C., and Smithers, D. W. Cytological analysis of response of malignant tumours to irradiation as approach to biological basis for dosage in radiotherapy. *Brit. J. Radiol.*, 1946, *19*, 89–100.

TREATMENT OF ADVANCED CANCER INVOLVING THE EAR*

By CHARLES L. MARTIN, M.D., *and* JAMES A. MARTIN, M.D.
DALLAS, TEXAS

ALTHOUGH much has been written about the treatment of cancer of the skin it is our impression that malignant lesions involving the ear receive relatively poor care in general practice and we are in complete agreement with Pfahler and Vastine[10] who state that "a greater percentage of failures occur in the treatment of cancer in the region of the ear than in any other relatively superficial portion of the body." For this reason many such patients are applying to tumor clinics for treatment of recurrences following surgical procedures, the application of caustics, drugs or roentgen and radium therapy. Carcinoma of the ear may be said to be advanced when the lesion involves the entire ear, when invasion is observed in the auditory canal or the surrounding structures, or when metastatic lymph nodes can be felt in the cervical region. It is worthy of note that 72 per cent of 57 patients with these findings entering our clinic from 1939 to 1947 had been treated unsuccessfully elsewhere.

TREATMENT

No single therapeutic measure has been universally successful in our hands and various combinations of electrosurgery, roentgen therapy and radium therapy have been used. Some authors believe that irradiation necrosis in cartilage can be prevented by the utilization of proper techniques but this painful complication was observed in many of our cases following treatment received elsewhere, and it seems evident that many of those who use irradiation are not successful in preventing cartilage damage. Although heavy filtration reduces this damage to a minimum and we have used it on occasion with good results it is now our custom to remove all cartilage showing malignant invasion with electrosurgery before starting irradiation. This procedure produces immediate relief of discomfort, tends to shorten the healing period and seems to improve the chance of cure. Certainly it should be carried out immediately in those cases showing malignant tissue growing about an area of irradiation necrosis.

After local anesthesia has been induced with butyn (0.75 per cent) the diseased portion of the ear is clamped in a hemostat and removed rapidly with the cutting current. The electrode consists of a large darning needle held in a long insulated handle. The incision is made through normal tissue well outside the malignant area. If a bleeding vessel is observed a coagulating current is applied for a few seconds through a hemostat which is immediately removed. The wound is never sutured and rapid healing is the rule if the cartilage does not protrude above the skin edges. For this reason the cartilage is always trimmed down well below these edges with a pair of sharp curved scissors. When the skin is allowed to heal over protruding cartilage the resulting stump is very tender and the patient cannot tolerate even slight pressure over it. Very large lesions often necessitate the removal of the entire auricle and the deeper portions must be extirpated by blunt dissection. When possible a portion of the upper auricle is left in place so the glasses may be worn with ease. In certain instances active carcinoma is observed growing about the edges of a slough produced by over-irradiation of an area situated near the ear. An attempt is made to cut away all of the devitalized tissue with sharp curved scissors at the same time that the diseased cartilage is removed.

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FIG. 1. Large squamous cell carcinoma, Grade 1, involving the ear, adjoining structures and auditory canal, treated by electrosurgery and radium needle implantation. The lower photographs were made six weeks and nine months following treatment. The implantation required eight 2.4 mg. and three 1.33 mg. radium needles.

Poor results following surgery alone are due to the extension of the malignant process into the tissues adjacent to the ear and the procedures described above are looked upon merely as proper preliminary measures which prepare the patient for radiation therapy. Radical operations designed to remove all of the deep-seated cancer not only fail to bring about this result in many instances but frequently damage the parotid gland and produce a facial paralysis.

Immediately after the completion of the operation a plan of irradiation should be instituted designed to completely eradicate all of the residual cancer. Although we favor the use of radium, good results have been obtained in skin cancer with a divided dose roentgen technique[8] described in 1935. A daily dose of 315 roentgens, measured in air, is given to a 10 by 10 cm. field until twelve doses are given using 200 kv., a target-skin distance of 50 cm. and a filter of 0.5 mm. of copper and 1.0 mm. of aluminum. The total irradiation given amounts to 3,780 r but calculations published in a recent article[7] indicate that the effective dosage in the depths of a tumor measuring 2.0 cm. in thickness becomes 2,176 r with backscatter or 3.2 threshold erythema doses when due allowance is made for the time factor. In 1935 Merritt and Rathbone[9] published data showing that the incidence of cartilage necrosis was markedly reduced when a minimum filtration of 2.0 mm. of copper or its equivalent was substituted. This valuable change in technique was soon adopted in our clinic. These authors used 220 kv. with a target-skin distance of 25 cm. and for an area measuring 1 by 1 to 3 by 3 cm. administered 6,000 r in nineteen days using a daily dose of 350 r, measured in air. By applying the methods advocated by Quimby and MacComb[11] and allowing for the effect of the time factor, the dose delivered to the surface amounts to approximately 3.8 T.E.D. With the same factors they administered a total of 4,500 r to areas measuring 10 by 10 to 15 by 15 cm. in twenty-two days at the rate of 200 r per day. This technique delivers approximately 3.7 T.E.D. to the depth of a tumor measuring 2.0 cm. in thickness. Although we have adopted the increase in filtration we have continued the use of a dose of 3.2 T.E.D. given in two weeks which we believe to be as effective as 3.7 T.E.D. given in approximately three weeks.

Heavy filtered radium therapy given entirely with surface applicators is advocated by Pfahler and Vastine[10] while Driver and Cole[1] favor the use of implanted low intensity radium needles. The latter method is our choice because dosage calculations are easier, the approximation of the radioactive sources to the diseased tissue is more accurate and the time of treatment is shorter. The needles used in our clinic have been fully described in previous articles.[2,4,6] They are made of platinum, have a wall thickness varying from 0.5 to 0.6 mm. and contain 0.6 to 0.8 mg. of radium per centimeter of active length. The needles found most useful have active lengths of 0.5, 1.5 and 4.0 cm. and contain 0.66, 1.33 and 2.4 mg. of radium, respectively. They are inserted into the malignant areas in patterns which deliver doses varying from 6,000 to 12,000 gamma roentgens to all of the cancer cells in a period of seven days. In most cases electrosurgery leaves a layer of tissue for implantation and the method used in dosage calculation is described in a recent article.[7] When the malignant tissue extends into the outer portion of the auditory canal, 0.66 mg. needles are inserted vertically into the walls of this passage.

Metastatic lymph nodes in the neck are treated with a combination of implanted low intensity radium needles and roentgen therapy using a technique described in previous articles.[3,5] A layer of low intensity needles is placed in the lymphatic bed containing the palpable nodes so that they deliver the same dose as that used for the primary lesion and 350 roentgens are then administered daily to the same area with 220 kv. roentgen-ray equipment until a total dose of 2,100 roentgens has been given while the needles are in place. A primary filter of 2.0 mm. of copper or its equivalent

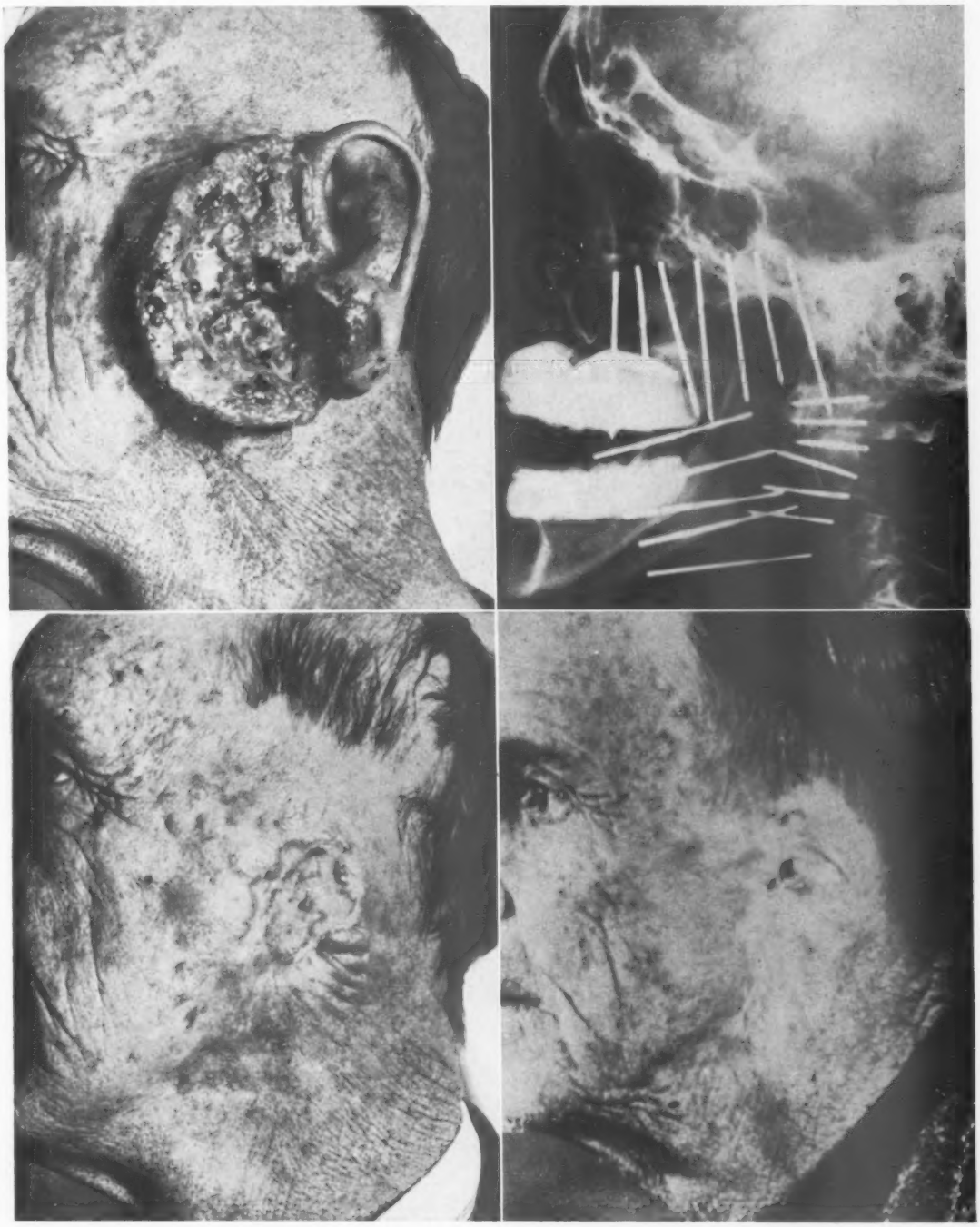

FIG. 2. Large squamous cell carcinoma, Grade 2, of the face which extended beneath the entire ear, treated by electrosurgery and radium needle implantation. The lower photographs were made six weeks and three years after treatment. The implantation required twelve 2.4 mg. and six 1.33 mg. radium needles.

is used with a target skin distance of 50 cm. Each needle is sutured in place and the wound is dressed daily with boric acid ointment. All needles are removed at the end of seven days and boric acid ointment dressings are continued until healing has taken place. When good results are obtained the wound is usually healed in six weeks to

FIG. 3. Mixed squamous cell and basal cell carcinoma of the face involving the lower half of the ear treated by electrosurgery and radium needle implantation. The lower photographs were made six months and three and a half years after treatment. The recurrence in front of the ear was successfully treated with divided dose roentgen therapy given six months after the radium implantation.

three months, but occasionally a longer period is required.

Extension of the malignant process into the underlying bone makes the prognosis very poor and no cases of this type have been completely cured in our clinic. However, definite improvement has been produced with the heavily filtered, divided dose roentgen-ray technique described above. No radium needles are used in such cases.

COMPLICATIONS

The intensive irradiation advocated by us depresses the function of the parotid

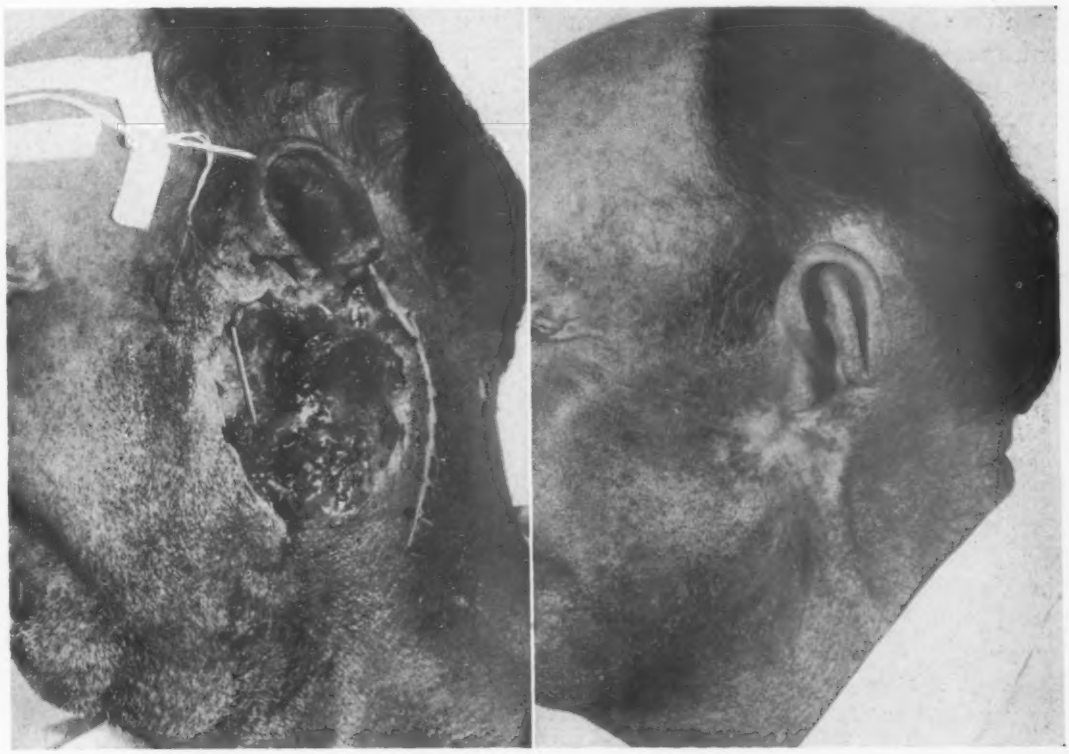

FIG. 4. Large deeply ulcerated squamous cell carcinoma, Grade 4, of the face involving the lower half of the ear treated with electrosurgery and radium needle implantation. Twelve 2.4 radium needles were implanted as shown in the photograph on the left. The photograph on the right was made five years later.

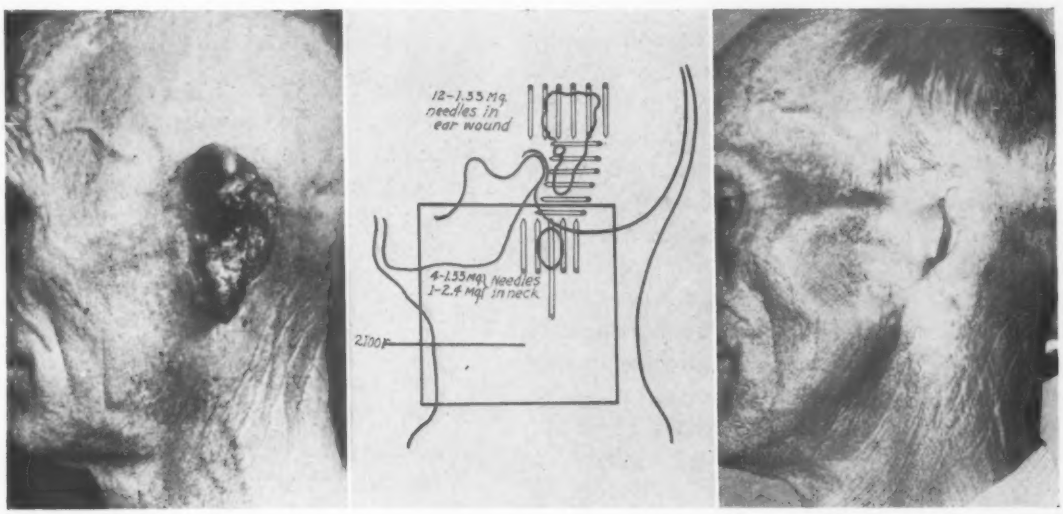

FIG. 5. Squamous cell carcinoma, Grade 2, involving the entire ear with a palpable node in the neck, treated by electrosurgery and radium needle implantation. The node was treated by a combination of radium needles and roentgen therapy. When the photograph on the right was made five months after treatment the gland was not palpable.

gland on the treated side for long periods of time and the patients complain of some dryness of the mouth, but the seventh nerve is never damaged and in no instance has a facial paralysis been observed after treatment. The first course of radiation therapy should always be designed to produce a cure and, as a rule, such treatment is not used a second time. If, as sometimes happens, large lesions are not completely eradicated and small recurrences are observed in the wound after healing they are destroyed with electrocoagulation. The skin behind the ear lies in close contact with the underlying bone and a slight overdosage in this region may produce a slough. Alvagel has proved useful in the treatment of this complication but in some instances a partial denudation of the outer surface of the mastoid has persisted. Although this end result is unsightly it seems to produce no real harm. When the surface of the bone is severely damaged it will eventually separate after which complete healing may occur.

As already stated any damaged cartilage in the treated area must be removed. The over-irradiation of a relatively small lesion on the anterior surface of the auricle with low voltage roentgen rays sometimes brings a patient into the clinic because of the severe pain produced by partial necrosis of the underlying cartilage. This complication can be quickly relieved by the careful removal of a button of cartilage from the treated area. If the skin on the posterior surface is left intact healing occurs rapidly and the cosmetic result is good.

FIG. 6. Deep-seated basal cell carcinoma extending into the auditory canal and beneath the ear treated with electrosurgery and radium needle implantation. The middle photograph and the one on the right were made six weeks and one year after treatment.

RESULTS

During the years 1939 through 1947 a series of 57 patients with advanced cancer of the ear has been admitted to our clinic. For the purpose of statistical investigation 35 of these cases treated three to seven years ago were studied. In 2, biopsy revealed mixed squamous cell and basal cell carcinoma but in the others these two types of cancer were about equally divided. The carcinoma involved the entire ear in 12 cases and extension well beyond the auricle was observed in 24 cases. The auditory canal was invaded in 7 patients and cervical nodes were palpable in two.

Only 9 of these patients are known to have died of cancer and 2 are still alive with some evidence of the disease present. Complete primary healing was obtained in

22 (63 per cent) and 18 (51.4 per cent) have remained well and free of disease for three to seven years of observation.

SUMMARY

Cancer involving the ear receives very poor care in general practice. Techniques are described which salvaged half of a series of 35 advanced cases most of which had been treated unsuccessfully elsewhere.

3501 Gaston Ave.
Dallas, Texas

REFERENCES

1. Driver, J. R., and Cole, H. N. Treatment of epithelioma of the skin of the ear. Am. J. Roentgenol. & Rad. Therapy, 1942, *48*, 66–75.
2. Martin, C. L. Small radium needles versus radon implants. Am. J. Roentgenol. & Rad. Therapy, 1932, *27*, 240–248.
3. Martin, C. L. Treatment of metastatic cervical lymph nodes. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 819–833.
4. Martin, C. L. Weak radium needle technique in carcinoma of the cheek. Am. J. Roentgenol. & Rad. Therapy, 1940, *43*, 226–236.
5. Martin, C. L. Treatment of metastatic cervical lymph nodes with irradiation. *Tr. Sect. Laryng., Otol. & Rhinol., A.M.A.*, 1940, pp. 86–108.
6. Martin, C. L. The layer technique in radium needle therapy. Am. J. Roentgenol. & Rad. Therapy, 1942, *48*, 377–383.
7. Martin, C. L. The time factor in radiation therapy. Am. J. Roentgenol. & Rad. Therapy, 1948, *59*, 1–8.
8. Martin, J. M., and Martin, C. L. Modified "Coutard" roentgen therapy. *J.A.M.A.*, 1935, *104*, 605–609.
9. Merritt, E. A., and Rathbone, R. R. Treatment of epithelioma involving cartilage using 220 k.v.p. and heavy filtration. *Radiology*, 1935, *24*, 701–707.
10. Pfahler, G. E., and Vastine, J. H. The treatment of cancer in the region of the ear. Am. J. Roentgenol. & Rad. Therapy, 1937, *37*, 350–357.
11. Quimby, E. H., and MacComb, W. S. Further studies on the rate of recovery of human skin from the effects of roentgen- or gamma-ray irradiation. *Radiology*, 1937, *29*, 305–312.

MALIGNANT TUMORS OF THE CHEEK IN CHILDREN*

REPORT OF TWO CASES

By GRANT E. WARD, M.D., *and* E. RODERICK SHIPLEY, M.D.
BALTIMORE, MARYLAND

MALIGNANT tumors of the cheek in children are relatively uncommon. Helmholz[4] of the Mayo Clinic has reported 750 cases of malignant neoplasms in children under fifteen years of age. Of these, 7.47 per cent, or 56 cases, occurred in the "intra-oral and neighboring regions." Of 218 cases of childhood cancer observed at Memorial Hospital in New York, Dargeon[2] reported 37 tumors of the head and neck, an incidence of 16.9 per cent. Malignancies of the face in children are about 100 times less frequent than in adults.[7]

The 2 cases summarized below are of interest since both were children under six years of age, both occurred in the same position and both presented a similar therapeutic problem. One of these children (Case 1) is living and well five years after irradiation and excision; the other infant (Case 11) died of the neoplasm less than a year after its appearance.

CASE REPORTS

CASE 1. V. M. (Univ. Hosp. No. 8453). This four year old colored female first presented herself to the Surgical Clinic of the University Hospital on November 10, 1943. In September, 1943, the child fell while at play and struck the right side of her face and nose. She had a moderately severe nose bleed, but no swelling was noticed. About ten days later, she again struck the right side of her face and, on examination, the mother noticed a tender, firm mass below the right eye. During the next two months, the mass gradually became larger and much firmer. The area was not painful.

On November 10, 1943, she was seen in the Surgical Clinic at which time it was thought that the mass was independent of the injury.

Examination revealed the eyes to be normal. A firm irregular mass measuring 5 by 3 by 2 cm. that appeared to be attached to the anterior wall of the right maxilla was easily seen and palpated. There was no evidence of inflammation. The tumor was hard, non-tender and extended upward toward the glabella and involved the right portion of the upper lip. The floor of the right nostril was elevated and covered by purulent crusts. The right inferior turbinate was extremely swollen, but the other turbinates were normal. The right maxillary sinus did not transilluminate.

A roentgenogram of the paranasal sinuses revealed no pathological process. On November 26, 1943, an aspiration biopsy was attempted through the lateral nasal wall, but no material was obtained.

The diagnosis of a malignant tumor—probably sarcoma—of the right antrum was made and the patient admitted to the University Hospital on November 30, 1943.

A roentgenogram of the paranasal sinuses, twenty-three days after the original film, revealed clouding of the maxillary sinuses probably due to sinusitis, but a tumor mass could not be excluded.

The mass was felt to be a malignancy of the right face, probably having its origin in the soft tissues over the right antrum. On December 5, 1943, a biopsy of this mass was taken under general anesthesia through an incision in the mucous membrane of the superior alveolar process down to the maxilla. With blunt dissection, the incision was carried over the mass which was cut into and found to be firm tissue with a white appearance. Grossly, it appeared to be sarcoma. A piece of tumor mass was removed for study. The patient's postoperative course was uneventful. The pathologist's report was as follows (Sp 47686) (Fig. 1).

Gross examination: The specimen consists of small pieces (4) of white firm tissue, each measuring 0.5 cm. in diameter. Not significant grossly.

Microscopic examination: Sections of the

* From the Departments of Oncology and Surgery, University Hospital, Baltimore, Maryland. Read before the American Association for the Study of Neoplastic Diseases, Washington, D. C., April 15, 1948.

material in this case show an edematous, partially hyalinized stroma infiltrated by tumor growth. The tumor cells are oval or somewhat spindle shaped. The nuclei contain much chromatin and stain deep blue. The cells invade the tissue in solid columns and as individual elements. This is a malignant anaplastic tumor. The exact classification is not determined. Metastasis from an adrenal neuroblastoma is a possibility which might be considered.

Impression: Malignant tumor.

Radiation therapy was thought to be the method of choice because of the age of the child and the location and size of the mass.

On December 14, 1943, the child was returned to the operating room and under general anesthesia, 19 platinum iridium needles, each containing 2 mg. of radium element, were implanted into the tumor, so distributed that the needles were about 1 cm. apart, in two layers—one layer being just anterior to the bony wall of the antrum and one layer being more superficial. Two of these needles were run across the upper lip beneath the skin where some firm tissue had been palpated.

The needles were left in place for a period of 157 hours, giving a total dose 2,993 milligram-hours, or 7 threshold erythema doses.

The needles were removed without difficulty, and the area healed well for about ten days. Following this, there was marked reaction of the skin and irritation of the eyelids with loss of the cilia. The skin over the area became quite red, hot, and swollen. The central portion of the area became necrotic and healed slowly to an area 2 by 3 cm. The patient was discharged from the hospital in excellent condition on February 1, 1944.

The child was followed closely in the Oncology Clinic and the area of slough healed almost completely. The patient had some inconstant pain in the area. On October 10, 1944, two months after her last visit, the child came to the clinic with the area almost completely broken down and secondarily infected. Nine days later, a large piece of dead bone (the zygoma) was removed, and following this, the area began to heal only to break down again in about three weeks. The patient was readmitted to the hospital on November 28, 1944, one year less three days from the first admission.

Examination at that time revealed a deep ulcer over the right face extending from the right nose to the level of the external canthus and from the lower right eyelid to the vermilian border of the upper lip. The lower lid was everted exposing some 3 mm. of reddened conjunctiva. Bony spicules arose from the depths of the wound which was bathed in a foul smelling, grayish pus. A deep sinus drained almost constantly from the upper medial border of the ulcer. The lateral wall of the right nostril was eroded, the wall being formed by a dull gray sequestrum. There was a profuse purulent discharge into the right nostril. Two upper right deciduous molar teeth were present, but the upper right canine and both incisors were absent. The patient's temperature was spiking to 102° F. every day.

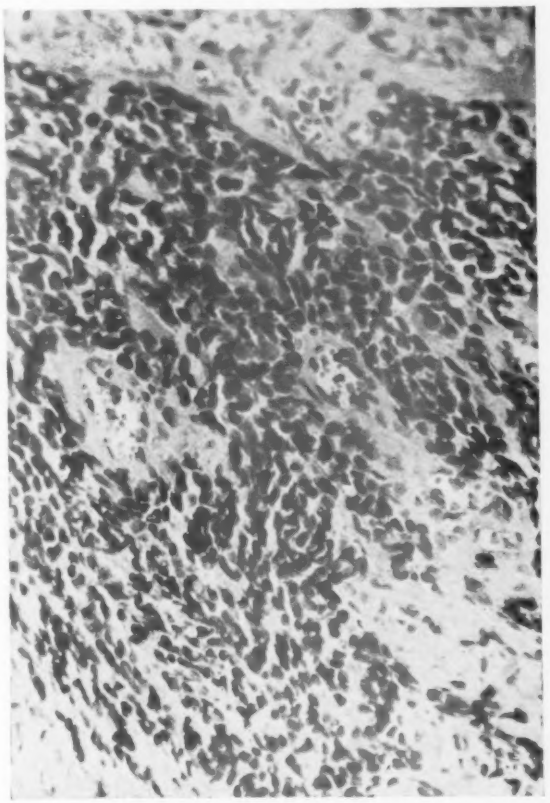

Fig. 1. Case 1. Photomicrograph of anaplastic malignant tumor.

The area was cleaned with hot, wet normal saline dressings directly to the ulcer. The right eye was protected by ophthalmic sulfathiazole ointment.

On December 8, 1944, under general anesthesia, the area was cleaned with alcohol and the anterior and medial bony walls of the maxillary sinus were lifted out en masse. The sinus was filled with a gray cheezy material that had

a very offensive odor. Portions of the alveolar process of the right maxilla were rongeured away and all remaining upper right teeth—both permanent and deciduous—removed. The posterior, superior, and lateral walls of the antrum were found covered by healthy mucous membrane. The area was packed with iodoform gauze.

The child was much improved after this, pain decreased and the odor was no longer offensive. The iodoform gauze was removed on the fourth postoperative day, and hot, wet compresses started. The area healed satisfactorily.

The defect (Fig. 2) was closed (Dr. E. A. Kitlowski) by tube grafting from the lateral aspect of the chest. The graft took well and the child was discharged as improved on June 17, 1945. Repeated biopsies of the area prior to grafting showed no evidence of the original growth.

FIG. 2. Case 1. Defect in face following treatment with 7 threshold erythema doses of radium given by interstitial route.

The patient has been followed in the outpatient department and has no evidence of recurrence. At present, the graft is excellent, but there is a marked ectropion, right, and a pulling up and out of the right side of the nose and upper lip due to scar tissue (Fig. 3). Further plastic repair is to be carried out in the near future. An early opacity of the right lens is questionably present and is probably an irradiation cataract.

CASE II. J. P. (Union Mem. Hosp. No. 105020). A small swelling about 2.5 or 3 cm. below the left lower eyelid was first noticed by the parents when this child, a white female, was about eight months old. Apparently, there was no birthmark or mole in the region. There was a history of a questionable injury while the child was playing, but there was no break in the skin. This tumor was removed surgically (Dr. H. A. Bailey, Charleston, W. Va.) when the child was ten months of age. The pathological diagnosis was "embryonic carcinoma." In the same month, five 15 mg. radium tubes were inserted into the wound (Dr. E. W. Squires, Charleston, W. Va.). The tubes were spaced about 1 cm. apart and were allowed to remain in place for five hours, a dose of 375 milligram-hours. From August 25 to September 4, 1942, she was given roentgen therapy, 200 roentgens per day for a total of 1,800 r. The factors used were 200 kv. at 50 cm. skin target distance, through a 3 cm. portal with 0.5 mm. copper filter.

A recurrence was noticed in December, 1942—four months after the original tumor was removed. At that time, the patient appeared healthy, had not lost weight, was lively and played about as a normal child. There was a single well healed scar parallel with the left lower eyelid and about 2.5 or 3 cm. below it. No local recurrence was seen in the scar. Above and medial to the scar, a mottled redness and swelling was noticed, especially below the inner half of the lid. Beneath the skin in this area, there was a hard lump which was fixed to the nose, but could be rocked back and forth. The temporal half of the lower lid was edematous and the nasal half showed some infiltration. There were no enlarged cervical glands.

FIG. 3. Case 1. Defect closed by plastic repair. Further improvement in appearance is expected by contemplated operations.

A roentgenogram of the antrum and skull was reported as showing a slight hyperplastic sinusitis, but no definite evidence of bone involvement in the left antrum. The roentgenograms of the skull were negative.

Because it was felt that this tumor was probably radioresistant, and because of fear of damage to the eye and bones of the face, it was advised that excision and immediate plastic repair be attempted.

Operation December 14, 1942 (patient was not under our care at the time) revealed that the growth had penetrated the nasal and maxillary bones. No line of cleavage was found. As much of the tumor and periosteum were removed as possible. Because of the extent of the tumor, it was felt that removal of the bony structures was not justified since this tumor had progressed beyond control.

Pathologic Report (Sp 24180) (Fig. 4). There is a rather mixed structure of large masses of small deeply staining cells, with round and oval spaces, suggesting either lymph spaces or an attempt at gland formation. This same kind of cell has infiltrated a dense hyalin fibrous tissue such as we see in mixed tumors of salivary origin. In some areas these cells stain rather darkly. Impression: Low grade malignant tumor arising from aberrant salivary tissue.

COMMENT

Sarcomas are thought to be far more common in childhood than in adult life. Helmholz[4] reports an incidence of 97 per cent sarcomas and 3 per cent carcinomas in 714 childhood malignancies. In a series of 16,565 malignancies, Pack and Lefevre[9] report 26.7 per cent were in patients under twenty-five years of age whereas 1.2 per cent of the carcinomas were in patients younger than twenty-five years. Thus sarcomas are twenty-two times as frequent as carcinomas in persons under twenty-five years of age.

Friedman and Rubenfeld[14] have reported 5 cases of cancer in children under fifteen years of age including 2 spindle cell sarcomas of the mouth and cheek. Sarcomas arising from the soft tissues of the face are not uncommon, but these tumors in general are found to be of a rapidly growing and highly malignant nature leading to the early death of the child.

In adults, malignancies of the face tend to occur in areas of chronic irritation and are usually more slowly growing and well differentiated, but in children the malignancy may occur in any area and tends to be more rapidly growing, more rapidly fatal, and more anaplastic.

Salivary tumors occur in children and infants, but are much more common in adults. Pack and Lefevre[9] report that 0.81 per cent of mixed tumors of the parotid gland occur in children under four years of age and that 2.43 per cent of these tumors occur under the age of fourteen years. Salivary tumors have been reported as occurring at the age of six weeks,[3] eleven months,[10] and one year.[6,9] About 10 per cent of the tumors which show the typical histopathologic picture of a mixed tumor of the salivary glands are found outside of the parotid, sublingual and submaxillary glands.[8]

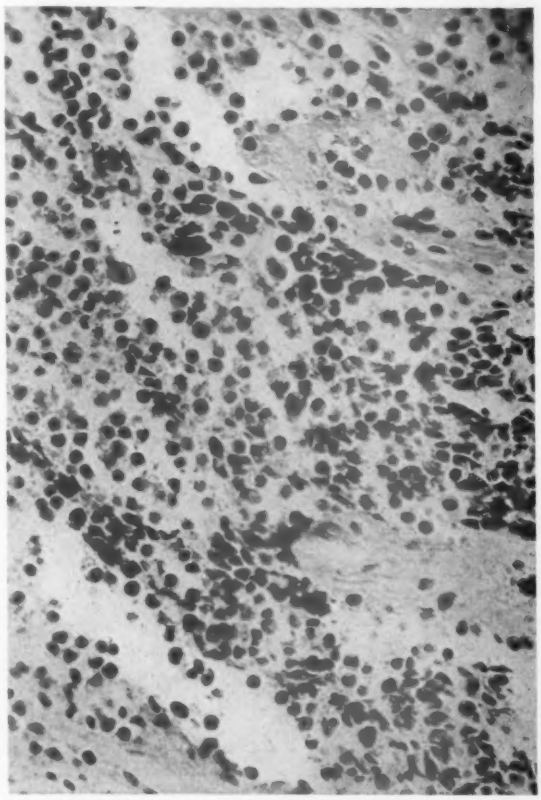

FIG. 4. Case 11. Photomicrograph of tumor. Note a more adenomatous arrangement than seen in the tumor of Case 1.

Many authors[1,6,11] have reported the presence of normal salivary tissue in the cheek explaining the origin of salivary tissue tumors outside of the glands proper. Wood[13] states that 25 per cent of all mixed salivary tumors become malignant, a figure that corresponds to the 28 per cent reported by Kuttner.[5] Reports of malignancies arising from aberrant salivary tissue in children have not been found in the literature. Pack and Lefevre[9] report the occurrence of a plexiform epidermoid carcinoma of the parotid region in front and below the right ear in a boy, aged four. In spite of two attempted surgical excisions and palliative radium therapy, the child succumbed to the malignancy six months after its appearance.

The therapy used in these 2 cases is of interest in view of the results obtained. The older child (Case I) received a large and relatively early course of radium therapy. The dose was a necrotizing one and has caused considerable deformity of the eyelid and upper lip, but with one or more plastic procedures, a good cosmetic result is to be expected. She has had no recurrence and is living a normal life and is doing well in school, five years later. The infant (Case II) received a relatively small dose of radiation, but the process continued and caused the death of the child. The favorable result obtained in Case I is due in part to several factors: the localized nature of the tumor, the early use of a large dose of radium, and the sensitivity of the tumor to radium.

Although salivary tumors of the cheek are rare, the possibility of their occurrence should be recognized and early therapy instituted. Sarcomas and malignancies developing in aberrant tissue in children are rapidly fatal and hope of cure is inversely proportional to the length of time between the appearance of tumor and institution of adequate therapy.

Grant E. Ward, M.D.
214 Medical Arts Bldg.
Baltimore 1, Md.

E. Roderick Shipley, M.D.
Medical Arts Bldg.
Baltimore 1, Md.

REFERENCES

1. CURR, J. F. Salivary-gland tumour of the upper lip. *Brit. M. J.*, 1945, *2*, 605.
2. DARGEON, H. W. Malignant tumors in childhood. *J. Pediat.*, 1939, *15*, 317–326.
3. DUTHOIT. Cited by Ahlbom, H. E. Mucous- and salivary-gland tumours. *Acta radiol.*, 1935, supp. 23, pp. 1–452.
4. HELMHOLZ, H. F. Malignant neoplasms in childhood. *Proc. Staff Meet., Mayo Clin.*, 1931, *6*, 721–724.
5. KUTTNER. Cited by Blair, V. P., and BYARS, L. T. In: Lewis' Practice of Surgery. Diseases of salivary glands. Edited by Waltman Waters. W. F. Prior, Inc., Hagerstown, Md., 1947.
6. MCFARLAND, J. Ninety tumors of the parotid region in all of which postoperative history was traced. *Am. J. M. Sc.*, 1926, *172*, 804–848.
7. MARTIN, H. E. Cancer of head and neck in children. *J. Pediat.*, 1939, *15*, 363–371.
8. MOORE, R. A. A Textbook of Pathology. W. B. Saunders Co., Philadelphia, 1945.
9. PACK, G. T., and LEFEVRE, R. G. Age and sex distribution and incidence of neoplastic diseases at Memorial Hospital, New York City, with comments on "cancer ages." *J. Cancer Research*, 1930, *14*, 167–294.
10. PAILLER. Cited by Blair and Byars.[5]
11. PATEY, D. H. Mixed tumours of the salivary glands. *Brit. J. Surg.*, 1930, *18*, 241–258.
12. ROBBINS, G. F. Tumors of salivary gland origin. *Surgery*, 1943, *14*, 924–930.
13. WOOD, F. C. Tumors of the salivary glands. *Ann. Surg.*, 1904, *39*, 57; 207.
14. FRIEDMAN, M., and RUBENFELD, S. Malignant neoplasms of the upper respiratory tract in the young. *Am. J. Cancer*, 1934, *22*, 786–800.

VOL. 60, NO. 6

CANCER OF THE LOWER LIP

SURVEY OF THE END RESULTS OF TREATMENT; ALL CASES TREATED AT THE BROOKLYN CANCER INSTITUTE 1930 THROUGH 1944

By WILLIAM E. HOWES, M.D., *and* JOSEPH ROSENSTEIN, M.D.
BROOKLYN, NEW YORK

IN THE fifteen years from 1930 through 1944, 112 cases of cancer of the lower lip applied for treatment at the Brooklyn Cancer Institute. This report continues the follow-up on cases reported by Howes and LaRosa[3] and incorporates additional cases treated since 1940. Whenever possible, all patients were traced to 1947, allowing a minimal follow-up interval of two years and a maximum of fifteen plus years.

Lesions arising on the lower lip are on an exposed surface and accessible to biopsy, pathological proof in this series is therefore 100 per cent.

RACIAL AND HEREDITARY TENDENCIES

In the existence of the Brooklyn Cancer Institute not a single member of the colored race has applied for treatment of cancer of the lip. This in spite of the fact that there is a large Negro population in Brooklyn and fully 10 per cent of all clinic and hospital admissions are of this race. Members of the colored race are known to have a high resistance to all forms of skin cancer, including melanoma.

Other than the apparent racial resistance to lip cancer in the Negro, no hereditary factors were disclosed.

ETIOLOGY

(*a*) *Intrinsic Factor.* Only 2 of 112 patients are women (1.7 per cent). The fact that this disease is almost exclusively limited to members of the male sex, a phenomenon which holds true to a certain extent throughout the respiratory epithelium, such as the larynx and bronchus, leads to the deduction that action of male hormone or some substance related to the male hormone must be a dominant intrinsic causative factor which sensitizes the lip epithelium to various extrinsic irritants.

(*b*) *Extrinsic Factors.* The incidence of a single injury to the lip followed by development of carcinoma is almost unheard of. As previously noted, "only one man had been struck on the lip and had noted the nodule after the trauma; another patient remembered an insect bite at the site where the lesion appeared" (Howes and LaRosa[3]). No additional case reports suggesting a single trauma as a possible causative factor were uncovered.

Blood serological studies were made in almost 100 per cent of the series. Only 8 were reported to be strongly positive with 3 others borderline. Tertiary syphilis must have passed unrecognized in an additional small number of instances. With less than 10 per cent giving clinical or serological evidence of this disease, syphilis can hardly be considered in the etiology of lip cancer.

The frequency with which leukoplakic spots were found on the mucous membrane side, and the frequent presence of atrophic keratoses on the carmine surface of the same lip involved with cancer indicates that a neoplasm is apt to develop in the background of degenerative change (Fig. 1, *A* and *B*). Furthermore, most of these men had dirty mouths, such as dental caries and chronic inflammation of the gingiva. This, however, may be a coincidental finding as obviously a large number of individuals who have extensive intraoral sepsis will never develop lip cancer.

Fully 90 per cent of the men had smoked a pipe, cigars or cigarettes throughout many years. Neither of the 2 women had used tobacco in any form. Although smoking has increased among women fully 1,000 per cent in the last generation, there has been no corresponding increase in the incidence of lip cancer.

In this series, the men were usually of the

unskilled laboring class. As a rule, they have worked outdoors during most of their adult life. Their faces and lips have been exposed to sun, wind, sleet and cold. Chapping as a result of exposure is a common occurrence. Theoretically this repeated chapping with resultant attempt to repair sets up an ideal situation purported to favor the origin of cancer.

The lip does not possess that protective mechanism which is common to the rest of the epidermis, namely, the ability to build up pigment. Thus ultraviolet rays are not filtered out as they are on other body surfaces and they can therefore penetrate into the living malpighian and basal layers to take full carcinogenic effect. The protective action of lipstick is here admitted. The number of our young men who developed carcinoma of the lower lip after serving in the Tropics with the armed forces leads to an emphasis on the presence of a carcinogenic factor in solar radiation.

The peculiar immunity of the upper lip to these same extrinsic factors is difficult to explain, except to note that the sun's rays strike the upper lip less directly. In this series only one man had a corresponding lesion on the adjacent surface of the upper lip, a phenomenon seen so frequently in a similar pathological type of carcinoma arising on the vulva in the female.

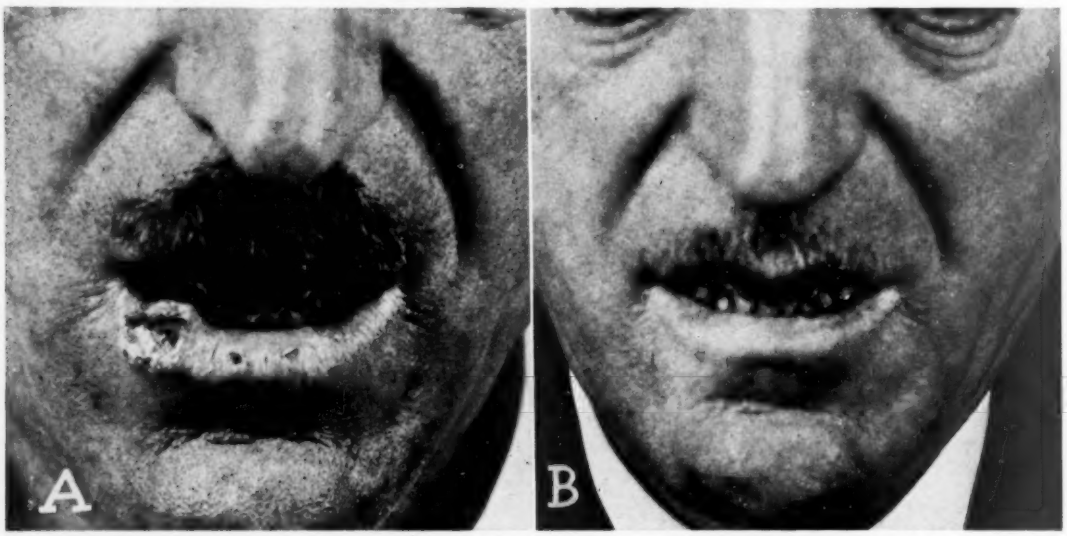

FIG. 1. M. C. Case C2629. *A*, presence of multiple lesions on carmine surface of lip, July 18, 1940. *B*, end result following roentgen therapy, January 8, 1942.

PATHOLOGY

The carmine surface of the lip is singularly devoid of the usual accessory skin structures common to skin. It is therefore logical that all carcinomas arising on the lip should be of the squamous cell type. Scanning the pathological reports in this series but one basal cell carcinoma is listed. The lesion in this instance appears to have arisen near the angle of the lip and may therefore have originated in the line of a fetal cleft, a site where basal cell lesions so frequently appear.

DIAGNOSIS

Because the lip is such a labile, actively moving part, any induration in and about a carcinoma quickly cracks to the surface and ulcerates. The buttonlike induration surrounding the base of such an ulceration may simulate chancre. Dark field examination and biopsy will differentiate one from the other. Antisyphilitic treatment should never be used as a therapeutic test without biopsy, as improvement following a few in-

jections of penicillin is prone to lull the therapist into apathy. A positive serological test for syphilis cannot rule out carcinoma.

Rhagades usually occur at or near the angle of the lip, while carcinoma more frequently arises somewhere within the middle third of the lip on its carmine surface. Rhagades should respond promptly to trial vitamin therapy. Biopsy will confirm clinical opinion.

Sunburn and herpes labialis can hardly be confused with carcinoma. Sunburn follows overexposure to sun. Protection from further exposure should result in healing within a week to ten days. Herpes labialis usually follows or accompanies a debilitating illness. The punctate vesicular character of the lesion in its early appearance does not simulate carcinoma.

A difficult problem of procedure is posed when biopsy of a suspicious lesion fails to demonstrate carcinoma. One such case was reported twice as benign, only to be diagnosed as carcinoma after surgical excision of the questionable lesion. Apparently in such instances infection with granulation tissue overlies the neoplastic cells.

TREATMENT

Successful treatment of cancer depends largely on early diagnosis. Those arising on the lip are no exception to this rule. A lesion on the lip should be obvious to the individual's sense of sight and touch. In spite of the obviousness of any lesion on the lip, the history of duration from the patient's statement in this series varied from one and a half weeks to twenty years. If the patient himself is indifferent, his family, friends and acquaintances cannot fail to observe its presence. The time elapsing between the recognition of the presence of a lesion and the seeking of medical aid averaged 13.7 months. As a corollary the majority of carcinomas when first seen were widely ulcerated, many measuring over 2

Table I

	Total	Average Duration Follow-up	Glandular Extension	Treatment Results	
				Success	Failure
Surgery	6	5 yr. 3 mo.	1	5	1
Roentgen therapy	55	4 yr. 10 mo.	8	44	11
Contact roentgen therapy	4	5 yr. 5 mo.	1	3	1
Radium mold	10	4 yr. 3 mo.	2	8	2
Interstitial radium	13	6 yr. 5 mo.	0	13	0
Surgery followed by roentgen therapy	6	4 yr. 8 mo.	1	5	1
Surgery followed by interstitial radium	2	1 yr. 2 mo.	0	1	1
Radium mold followed by roentgen therapy	2	1 yr. 9 mo.	2	0	2
Interstitial radium followed by roentgen therapy	12	4 yr. 5 mo.	6	5	7
Radium mold followed by interstitial radium	1	7 yr.	0	1	0
Roentgen therapy followed by interstitial radium and surgery	1	9 yr.	0	1	0
Totals	112		21	86	26

FIG. 2. P. Mc. Case 2317. *A*, appearance of lesion before roentgen therapy, March 18, 1940. *B*, height of reaction illustrating size and shape of area treated, May 2, 1940. *C*, end result, September 3, 1940.

cm. in diameter. Eleven of these individuals (10 per cent) had palpable submental, submaxillary or cervical glands at the time of their first visit. An additional 21 (18 per cent) developed palpable lymph nodes some time after treatment was instituted, a number of whom must have had unrecognized metastatic lymph node extension at the time of their original examination.

Carcinomas of the lower lip have been successfully eradicated by: (1) surgery, (2) irradiation, and (3) combined surgical and radiological procedures.

(1) *Surgery*. Surgery has its rightful place in the treatment of cancer of the lip. Such surgery, however, must be extensive and to succeed the surgeon must assure himself that he is able to excise tissue well beyond the obvious cancer zone. Closure should follow with suitable plastic procedure to prevent puckering, so-called "fish mouth" deformity. If submaxillary or cervical lymph nodes are involved, a further radical neck dissection may be indicated (Duffy[1]). Six cases were treated by surgery. One developed metastatic glands in the neck and died within six months. The remaining 5 cases are being followed through the clinic averaging over five years, a highly satisfactory result.

(2) *Irradiation*. The lip, by its superficial position and ease of approach, affords the radiologist many advantages, in that a cancerocidal dose can be delivered within a

FIG. 3. S. B Case H4082. *A*, appearance of lesion before therapy, September 17, 1940. *B*, end result of roentgen therapy, April 29, 1941. Note the metastasis in the submaxillary triangle.

Fig. 4. A. S. Case 6676. *A*, lesion before therapy, March 29, 1939. *B*, end result, November 9, 1939.

given interval of time and surrounding normal structures can be protected from injury.

(A) Roentgen irradiation (superficial and deep): The technique of roentgen therapy to the lip as carried out at the Brooklyn Cancer Institute has varied throughout the years. Those cases treated before 1936 received superficial therapy, i.e., 80 to 135 kv. with half-value layer of 1 to 3 mm. aluminum. The lesions were blocked within 0.5 cm. of the obvious cancer and a single dose of 4,000 to 6,000 roentgens (measured in air) delivered (Howes[2]). After careful study of these results it was decided to enlarge the treatment area to a V-shaped configuration, similar to the segment to be removed if surgery were contemplated (Fig. 2, *A*, *B*, *C*). To protect the mouth and mandible, a shield of lead impregnated rubber was inserted between the lip and alveolus. Furthermore, the single massive dose was broken up into eight to twelve fractionated daily treatments (Fig. 3, *A* and *B*).

The technical factors used are: 200 kv., Thoraeus filter, half-value layer of 1.8 mm. Cu, 30 cm. target skin distance, 600 r in air delivered daily. The effort is made to deliver a total air dose of 7,200 r within two weeks (Paterson[6]). Recurrences have taken place when the dose was reduced to 4,500 r or less. An intense radiation reaction results from such a series of treatments; this

Fig. 5. S. R. Case 5891. *A*, appearance of lesion before therapy, July 1, 1940.
B, end result, January 23, 1941.

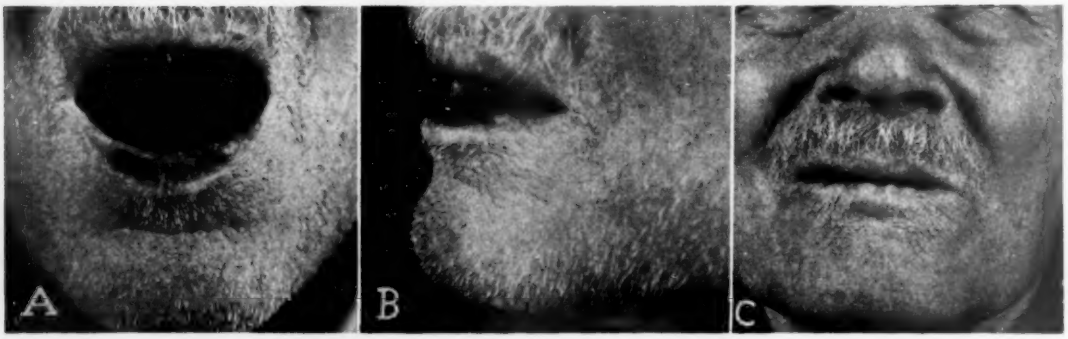

FIG. 6. A. B. Case C6197. *A*, appearance of lesion before therapy, April 18, 1940. *B*, lateral view before therapy. *C*, end result October 14, 1940.

is followed by healing with scar formation. Using this technique, necrosis with failure to heal has never complicated the end result (Fig. 4, *A* and *B*). Filtration is added theoretically to minimize telangiectasis and scar atrophy (Fig. 5, *A* and *B*). Extensive lesions involving most of the lower lip have been successfully treated by this technique and the resultant scar is soft and pliable and does not give the patient any discomfort (Fig. 6, *A*, *B*, *C*).

Fifty-five cases were treated by roentgen therapy.

Of the 11 cases treated by a single massive dose of relatively unfiltered radiation, 6 developed metastases. These cases (males) were listed as failures; most were followed through the clinic for approximately one and a half years when they were either lost to follow-up or died.

Forty-four cases received divided dose roentgen therapy as described above. The primary carcinoma was destroyed in each of these 44 instances. Two of this subgroup, however, later developed cervical glandular metastases and a block dissection of the neck was carried out (Fig. 7, *A* and *B*). Both these cases have reported back to the out-patient clinic, a duration of nine and ten years respectively.

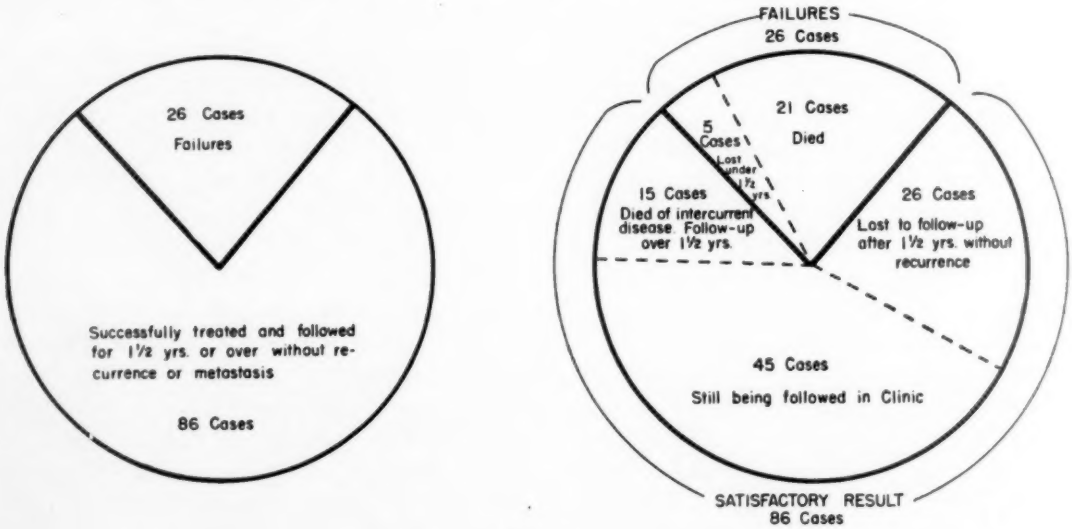

FIG. 7.

(B) Contact roentgen therapy: Four individuals were treated by the air-cooled contact roentgen therapy using 45 kv., 2 ma., 2.1 cm. target skin distance, half-

value layer 3 mm. aluminum, as described by Howes and Camiel.[4] The lesions were blocked off to about 0.5 cm. of their edge by lead foil. Three of these patients whose lesion measured over 1 cm. in diameter received 15,000 r in air delivered to the lesion at one sitting. These patients visit the clinic today, they show no evidence of recurrence, a follow-up interval of six years. The fourth was given a much greater surface roentgen dose, as his lesion was larger and thicker. The theory is to deliver a carcinolethal dose to the base of the neoplasm estimating the absorption within the superficial layers of the growth. This case developed cervical metastases which were treated by high voltage roentgen therapy augmented by interstitial radium. He died four years after the onset of treatment.

(C) Radium

(a) Mold: A radium mold was applied in 10 instances. By drawing the lip forward, the tubes can be arranged within a wax mold to crossfire the lesion both from the buccal mucosa and the external surface of the lip. The distance from the radium sources to the lip surface is 1 cm. (Fig. 8, *A* and *B*). The element tubes are filtered by 1 mm. of platinum. According to the extent of the lesion the total dose varied from 1,200 to 2,500 milligram-hours. Gamma roentgens have been computed since 1939, following knowledge and acceptance of Paterson and Parker tables,[5] tumor dose being estimated to 6,000 gamma roentgens. Three of those treated by radium mold already had or later developed glandular extension. One of these cases with glandular extension was later controlled by the injection of interstitial radium and radon into the metastatic nodes (proved by biopsy to be carcinoma). This patient survived eleven years without further spread. The other 2 patients died nine months and one and a half years later. The remaining 7 cases are recorded as having satisfactory end results. When last seen they were without evidence of recurrence, from two to sixteen years.

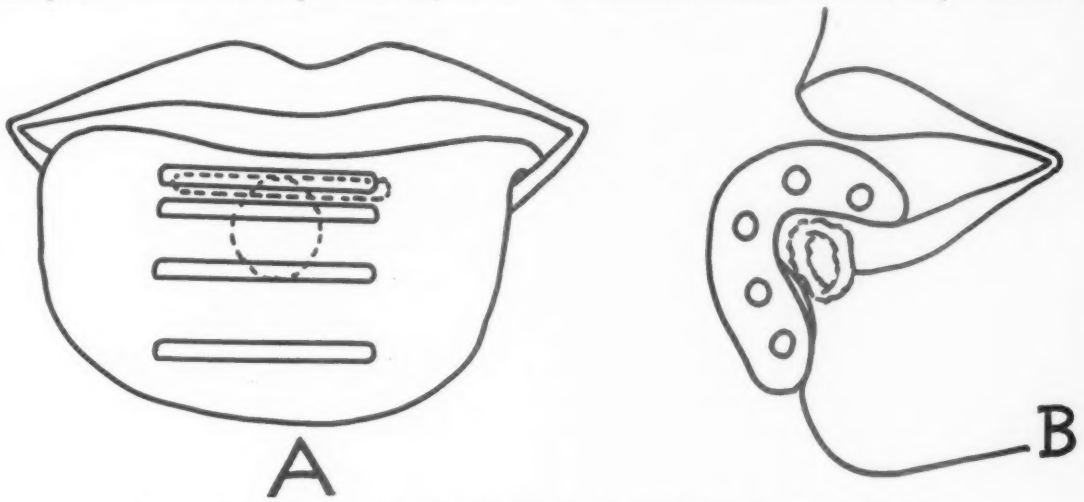

Fig. 8. Schematic drawing of radium mold. *A*, anterior view; *B*, lateral view.

(b) Interstitial radium: Thirteen cases were treated by the insertion of radium needles or radon seeds in and about the lesion. When needles were used they were inserted from 0.5 to 1 cm. apart, often in two planes: one on the buccal, the other on the skin side (Fig. 9, *A* and *B*). The minimal gamma roentgen dose in all cases was calculated to 6,000 gamma roentgens. Not a single failure occurred in this group; all have survived a period averaging five to six years. Some still visit the clinic after a twelve years, others have been lost or have died from some intercurrent disease after several years of follow-up. Even though results of interstitial radium treatments in this small series were so uniformly satis-

factory, it must be admitted that dosage in gamma roentgens varies markedly in intensity within a few millimeters of the radium sources. Success, therefore, must depend on the ability of the operator to accurately place such focal sources of radiation within the tissues to avoid over and under dosage. Trauma relative to inserting needles or seeds into an infected area must also be taken into consideration when comparing with other modes of treatment.

(3) *Combined Procedures.* Treatment by combined procedures indicates that the first treatment choice was unsuccessful, and recurrence or residuum was treated differently. Failure of the original modality to control the growth and substitution of another method of treatment would obviously tend to lower the percentage of satisfactory end results. Twenty-four cases are recorded as treated by some combined method of therapy as follows:

(A) Surgery and roentgen therapy: Excision either followed or preceded by roentgen therapy is recorded in 6 instances. Five of these had a satisfactory end result though 2 were lost track of after two and five years respectively. One died of other causes after a seven year follow-up in the clinic. Two still attend the clinic, a time interval of seven and eight years respectively. The only one listed as a failure in this subgroup developed cervical metastases and died within nine months.

(B) Interstitial radium and surgery: Two patients were treated by combining interstitial radium with surgery. Here again the inference points to failure of the original effort with the second form of treatment serving as a stop gap measure. One of the 2 was lost track of one and a half years after completion of this treatment (a satisfactory result was noted on his record at his last clinic visit). The second listed as a failure developed cervical metastases early; he died within nine months.

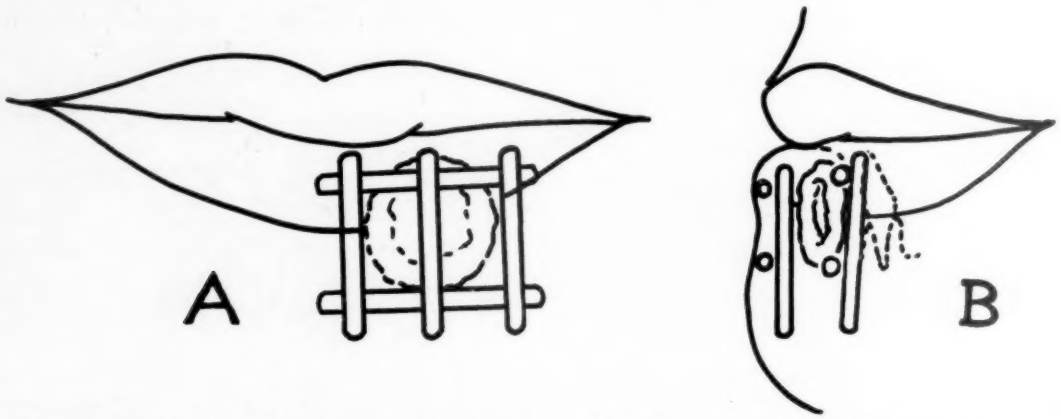

FIG. 9. Schematic drawing of arrangements of radium needles in interstitial treatment. Theoretically the central needle should be of lesser content. It is not always practical to insert needles both on the skin and mucous membrane sides of the lip. *A*, anterior view; *B*, lateral view.

(C) Surgery, roentgen irradiation and radium: One case only (treated in 1936) received roentgen therapy to a recurrence following surgery, and still later a small amount of radium was inserted into a further extension. In spite of the obvious fallacy in the conduct of treatment, this patient has been followed in the out-patient clinic for a period of nine years without evidence of further recurrence.

(D) Radium and roentgen therapy: Twelve cases were treated by combined radium and roentgen therapy. Many of these lesions were extensive when first seen, though the incomplete destruction of the lesion by the original method employed must be considered as a mitigating factor in the unsatisfactory end result obtained.

However, 5 of these 12 obtained a satisfactory end result with no recurrence or metastases appearing to date. Six (50 per cent) who developed cervical metastases and the seventh lost early to follow up are all listed as unsatisfactory. Since 1939 the more accurate estimation of dosage and the more extensive therapeutic attack have obviated the necessity of any second therapeutic approach. The percentage of lymph gland spread has also been proportionately reduced.

TREATMENT OF METASTASES

Carcinoma of the lip apparently spreads but slowly to the regional lymph glands. Less than 10 per cent were known to have cervical metastases on admission though the average duration of knowledge of the lip lesion averaged over one year. Destruction of the primary lip lesion proved sufficient to eradicate the disease in the majority of cases (78 per cent). These statistics indicate that prophylactic irradiation or surgical block dissection of the neck is hardly indicated as a routine procedure. Before 1937, 7 cases were given prophylactic irradiation to the neck. The total roentgen-ray dosage delivered by present day concepts was insufficient to destroy any metastases, if present. By the same token neck surgery other than a radical block dissection is unwarranted. Radical neck dissection even though it carries low morbidity and low mortality can hardly be justified as a routine procedure when metastases are shown to occur in but 1 in 7 instances.

Eight patients (males) when first admitted were known to have glandular extension either to the submental area, submaxillary triangle, or anterior cervical lymphatics. The only one to gain a satisfactory end result received roentgen therapy to the lip followed by radical block dissection of the neck. On his last visit to the clinic nine years after treatment, he appeared to be free of disease. All others are recorded as failures: 2 with metastases refused further treatment, dying one and two years later. All the others (5) received some form of radiation either alone or in combination to the metastases; all died from nine months to two years after institution of therapy.

As shown in Table 1, 21 cases (18 per cent) developed glandular metastases following therapy to the primary lip lesion. Only 4 of the 21 (19 per cent) obtained a satisfactory result: 2 by radical neck dissection and 2 by radon seed implantation. One of the 2 who survives following surgery has been followed for a period of ten years; the other died of intercurrent disease seven years later. The most successful method of handling cervical lymph node extension appears to be by radical block dissection.

Technique of radon seed implantation is as follows: Radon seeds each 1 mc., filtration 0.3 mm. of gold are as evenly distributed within the involved gland as possible. The plan is to distribute these radiant sources approximately 0.5 cm. apart. Such a seeded gland is estimated to receive up to 9,000 gamma roentgens. Of the 2 patients who survived seeding of metastatic neck glands one is still being followed in the clinic after eleven years, the other died of intercurrent disease seven years later. The remaining 17 are recorded as failures. All were treated by roentgen therapy, interstitial radon, singly or in combination. From an analysis of these results, external irradiation in doses sufficient to preserve the overlying skin is insufficient to sterilize such glandular extension. Roentgen therapy must therefore be supplemented by interstitial irradiation, this in order to deliver a sufficient cancerocidal dose.

Summary of all Cases (*Table II*). Individual end results are noted as died, lost, and—those still under observation—clinic. Treatment end results are listed as satisfactory or failure. To be listed as satisfactory, the patient must have been followed at least a year and a half in the clinic without evidence of recurrence or glandular spread. Certain cases who have died of intercurrent disease after years of follow-up

TABLE II

SUMMARY OF ALL CASES

Year	Case	Treatment to Lip	Treatment to Neck	History	Duration of Follow-up	Glands on Admission	Metastatic Spread	End Result	Treatment Result
1930	3220	Radium mold	No	6 mo.	2½ yr.	No	Yes	Died	Failure
	3384	Surgery	Roentgen therapy	1 yr.	6 mo.	No	Yes	Died	Failure
1931	3489	Roentgen therapy + Interstitial radium	No	3 yr.	2 yr.	No	No	Lost	Satisfactory
	3852	Roentgen therapy	Roentgen therapy	6 mo.	1½ yr.	No	No	Lost	Satisfactory
	3960	Radium mold	Roentgen therapy	1 yr. 3 mo.	1½ yr.	No	No	Lost	Satisfactory
	4003	Radium mold	Roentgen therapy	4 mo.	3 yr.	No	No	Lost	Satisfactory
	4024	Radium mold	Roentgen therapy	2 mo.	16 yr.	No	No	Clinic	Satisfactory
1932	4083	Radon mold	Roentgen therapy	1 yr.	9 mo.	Yes	Yes	Died	Failure
	5332	Surgery + Interstitial radium	No	3 wk.	1½ yr.	No	No	Lost	Satisfactory
	5508	Roentgen therapy	Roentgen therapy	2 mo.	1 yr.	No	No	Lost	Satisfactory
1933	6668	Roentgen therapy	No	3 mo.	2 yr.	No	No	Lost	Satisfactory
	6085	Roentgen therapy	Roentgen therapy	3 yr.	3 yr.	No	No	Died	Satisfactory
	6251	Radium mold	No	6 mo.	8 yr.	No	No	Died	Satisfactory
	6409	Roentgen therapy	Roentgen therapy	6 wk.	12 yr.	No	No	Died	Satisfactory
	5973	Interstitial radon	No	6 mo.	12 yr.	No	No	Clinic	Satisfactory
	5192	Interstitial radon + Roentgen therapy	No	8 mo.	9 yr.	No	No	Died	Satisfactory
	6475	Radium mold + Roentgen therapy	Roentgen therapy	1½ mo.	9 mo.	No	Yes	Lost	Failure
1934	6921	Roentgen therapy	No	2 mo.	13 yr.	No	No	Clinic	Satisfactory
	6704	Interstitial radon + Roentgen therapy	Roentgen therapy + Interstitial radon	2 mo.	3 yr.	No	Yes	Died	Failure
	6733	Roentgen therapy	Roentgen therapy	3 mo.	5 yr.	No	No	Lost	Satisfactory
1935	8123	Radium mold + Interstitial radon	No	1 yr.	7 yr.	No	No	Lost	Satisfactory
	8282	Interstitial radium	No	6 mo.	2 yr.	No	No	Died	Satisfactory
	7612	Interstitial radium + Roentgen therapy	Roentgen therapy	2 yr.	2 yr.	No	Yes	Died	Failure
	8304	Roentgen therapy + Interstitial radium	No	2 mo.	12 yr.	No	No	Clinic	Satisfactory
	8005	Roentgen therapy	No	7 mo.	5½ yr.	No	No	Lost	Satisfactory
1936	8443	Radon mold	Interstitial radon	4 mo.	11 yr.	No	Yes	Clinic	Satisfactory
	8359	Surgery + Interstitial radium + Roentgen therapy	No	3 mo.	9 yr.	No	No	Lost	Satisfactory
	8722	Surgery + Roentgen therapy	No	6 mo.	4 yr.	No	No	Lost	Satisfactory
	8759	Radium mold + Roentgen therapy	No	3 wk.	3 yr.	No	Yes	Lost	Failure
	8523	Interstitial radium	Roentgen therapy	20 yr.	7 yr.	No	No	Died	Satisfactory
	8421	Radium mold	No	4 mo.	4 yr.	No	No	Lost	Satisfactory
	8510	Surgery + Interstitial radium	Interstitial radium + Roentgen therapy	8 mo.	9 mo.	Yes	Yes	Died	Failure
	8447	Roentgen therapy	No	3 mo.	3 yr.	No	No	Lost	Satisfactory
	8888	Roentgen therapy	No	4 mo.	9 yr.	No	No	Clinic	Satisfactory
	8731	Interstitial radon + Roentgen therapy	No	1 mo.	11 yr.	No	No	Clinic	Satisfactory
	8770	Interstitial radium	No	1 yr.	10 yr.	No	No	Clinic	Satisfactory
	8725	Roentgen therapy	Roentgen therapy	8 mo.	3 yr.	No	No	Died	Satisfactory
	8749	Interstitial radon + Roentgen therapy	Interstitial radium + Roentgen therapy	3 mo.	2 yr.	Yes	Yes	Died	Failure
	8567	Interstitial radium	No	3 mo.	3 yr.	No	No	Died	Satisfactory
1937	595	Roentgen therapy	Surgery	1 yr.	10 yr.	No	Yes	Clinic	Satisfactory
	558	Roentgen therapy	No	1 yr.	7 yr.	No	No	Lost	Satisfactory
	325	Roentgen therapy	No	6 mo.	2 yr. 9 mo.	No	No	Lost	Satisfactory
	122	Roentgen therapy	No	6 mo.	9 yr.	No	No	Clinic	Satisfactory

Table II—(*continued*)

Year	Case	Treatment to Lip	Treatment to Neck	History	Duration of Follow-up	Glands on Admission	Metastatic Spread	End Result	Treatment Result
1937	546	Surgery Roentgen therapy	No	16 mo.	7 yr.	No	No	Died	Satisfactory
	375	Interstitial radium Roentgen therapy	Surgery	8 mo.	7 yr.	No	Yes	Died	Satisfactory
	2036	Radium mold	No	6 mo.	7 yr.	No	No	Lost	Satisfactory
	47	Roentgen therapy	Surgery	10 mo.	9 yr.	Yes	Yes	Clinic	Satisfactory
	398	Roentgen therapy	Interstitial radium	10 yr.	1½ yr.	No	Yes	Died	Failure
1938	945	Interstitial radium	No	8 mo.	6 yr.	No	No	Lost	Satisfactory
	674	Roentgen therapy	No	3½ yr.	8 yr.	No	No	Clinic	Satisfactory
	1112	Roentgen therapy	No	4 mo.	8 yr.	No	No	Clinic	Satisfactory
	861	Interstitial radium	No	18 mo.	9 yr.	No	No	Clinic	Satisfactory
	1352	Roentgen therapy	No	2 mo.	9 yr.	No	No	Clinic	Satisfactory
	1380	Surgery Roentgen therapy	No	6 mo.	9 mo.	No	Yes	Died	Failure
	963	Interstitial radium	No	2 yr.	9 yr.	No	No	Clinic	Satisfactory
	1246	Interstitial radium Roentgen therapy	No	5 wk.	2 yr.	Yes	Yes	Died	Failure
	831	Interstitial radium	No	1 yr.	5 yr.	No	No	Lost	Satisfactory
	907	Roentgen therapy	Interstitial radon	3 mo.	7 yr.	No	Yes	Died	Satisfactory
	1035	Interstitial radium Roentgen therapy	No	6 mo.	1½ yr.	No	Yes	Died	Failure
	4357	Surgery	No	6 mo.	9 yr.	No	No	Clinic	Satisfactory
1939	2003	Roentgen therapy	No	10 wk.	8 yr.	No	No	Clinic	Satisfactory
	1773	Roentgen therapy	No	1 yr.	8 yr.	No	No	Clinic	Satisfactory
	1895	Radium mold	No	7 mo.	1 yr.	No	No	Lost	Satisfactory
	1912	Interstitial radium	No	3 yr.	2 yr.	No	No	Died	Satisfactory
	1922	Roentgen therapy	No	1¼ wk.	2 yr.	No	No	Lost	Satisfactory
	1452	Surgery Roentgen therapy	No	7½ yr.	8 yr.	No	No	Clinic	Satisfactory
	1741	Surgery Roentgen therapy	No	3 mo.	2 yr.	No	No	Lost	Satisfactory
	1852	Roentgen therapy	Roentgen therapy	5 mo.	1½ yr.	No	Yes	Lost	Failure
	1850	Roentgen therapy	No	7 wk.	3 yr.	No	No	Died	Satisfactory
	1565	Roentgen therapy	No	6 mo.	7 yr.	No	No	Died	Satisfactory
	1648	Roentgen therapy	No	5 yr.	1½ yr.	No	No	Lost	Satisfactory
	1411	Roentgen therapy	No	6 mo.	8 yr.	No	No	Clinic	Satisfactory
	1940	Roentgen therapy	No	6 mo.	8 yr.	No	No	Clinic	Satisfactory
	1035	Interstitial radium Roentgen therapy	No	6 mo.	1½ yr.	No	Yes	Died	Failure
	1742	Interstitial radium Roentgen therapy	Interstitial radium Roentgen therapy	4 mo.	1¼ yr.	No	Yes	Died	Failure
	1975	Interstitial radium	No	9 mo.	4 yr.	No	No	Lost	Satisfactory
1940	2629	Roentgen therapy	No	1 yr.	7 yr.	No	No	Clinic	Satisfactory
	2317	Roentgen therapy	Roentgen therapy	5 mo.	7 yr.	No	No	Clinic	Satisfactory
	2577	Roentgen therapy	No	2 mo.	7 yr.	No	No	Clinic	Satisfactory
	2308	Surgery Roentgen therapy	No	1 yr.	7 yr.	No	No	Clinic	Satisfactory
	2651	Roentgen therapy	No	3 wk.	7 yr.	No	No	Clinic	Satisfactory
	2961	Roentgen therapy	No	6 mo.	7 yr.	No	No	Clinic	Satisfactory
	6197	Roentgen therapy	No	7 yr.	5 yr.	No	No	Lost	Satisfactory
	2774	Roentgen therapy	No	2 mo.	4 yr.	No	No	Lost	Satisfactory
	2966	Interstitial radium	No	1 mo.	7 yr.	No	No	Clinic	Satisfactory
	6647	Contact therapy	Interstitial radium Roentgen therapy	10 mo.	4 yr.	No	Yes	Died	Failure
	4082	Roentgen therapy	Roentgen therapy	1 yr.	2 yr.	No	Yes	Lost	Failure
1941	3185	Roentgen therapy	No	5 mo.	6 yr.	No	No	Clinic	Satisfactory
	5613	Roentgen therapy	No	9 yr.	6 yr.	No	No	Clinic	Satisfactory
	3747	Contact therapy	No	2 yr.	6 yr.	No	No	Clinic	Satisfactory
	4096	Roentgen therapy	No	2 yr.	1 yr.	Yes	Yes	Lost	Failure
	4317	Contact therapy	No	1 yr.	6 yr.	No	No	Clinic	Satisfactory

TABLE II—(*continued*)

Year	Case	Treatment to Lip	Treatment to Neck	History	Duration of Follow-up	Glands on Admission	Metastatic Spread	End Result	Treatment Result
1941	3491	Contact therapy	No	3 yr.	6 yr.	No	No	Clinic	Satisfactory
	3385	Surgery	No	8 mo.	6 yr.	No	No	Clinic	Satisfactory
	3720	Surgery	No	6 mo.	6 yr.	No	No	Clinic	Satisfactory
1942	4233	Roentgen therapy	No	1 yr.	5 yr.	No	No	Clinic	Satisfactory
	5175	Surgery	No	8 mo.	5 yr.	No	No	Clinic	Satisfactory
	4281	Roentgen therapy	No	6 mo.	5 yr.	No	No	Clinic	Satisfactory
	4361	Surgery	No	2½ yr.	5 yr.	No	No	Clinic	Satisfactory
	5069	Roentgen therapy	Interstitial radium	2 mo.	1½ yr.	Yes	Yes	Died	Failure
	6005	Roentgen therapy	Roentgen therapy Radon seeds	1 yr.	1½ yr.	No	Yes	Died	Failure
	6221	Roentgen therapy	Roentgen therapy	1 yr.	2 yr.	Yes	Yes	Died	Failure
	4276	Roentgen therapy	No	6 mo.	5 yr.	No	No	Clinic	Satisfactory
1943	4800	Roentgen therapy	No	8 mo.	4 yr.	No	No	Clinic	Satisfactory
	4704	Roentgen therapy	No	6 mo.	4 yr.	No	No	Clinic	Satisfactory
	5018	Roentgen therapy	No	1 yr.	1 yr.	No	No	Died	Satisfactory
	6752	Roentgen therapy	No	6 mo.	2½ yr.	No	Yes	Died	Failure
	5798	Roentgen therapy	Interstitial radon Roentgen therapy	5 mo.	1½ yr.	Yes	Yes	Died	Failure
1944	7108	Interstitial radium	No	1 yr.	1½ yr.	No	No	Died	Satisfactory
	6864	Roentgen therapy	Roentgen therapy	1 yr.	9 mo.	No	Yes	Died	Failure
	6406	Roentgen therapy	Interstitial radon	3 mo.	1 yr.	Yes	Yes	Died	Failure
	5163	Roentgen therapy	No	4 mo.	3 yr.	No	No	Clinic	Satisfactory

but who have shown no evidence of recurrence in this interval are listed as satisfactory. Failure indicates inability to control the primary lesion or inability to destroy cervical metastases which may have appeared at any time during the follow-up period.

SUMMARY

In the fifteen year period, 1930 through 1944, 112 cases of proved carcinoma of the lip were admitted for treatment to the Brooklyn Cancer Institute.

A strong racial resistance was indicated by the absence of any lip lesion in Negro patients. A study of the histories failed to bring out any other evidence of hereditary influence.

The disease is almost entirely limited to the male and by inference it is suggested that the male hormone or some variant of this hormone may be the intrinsic etiological agent while the extrinsic factors can be many. Ultraviolet light is probably the most potent of these. Certainly smoking which is so frequently ascribed as a causative agent can be ruled out as so few lesions originate in the female though there has been a great increase in smoking among women in the last generation.

Differential diagnosis is not difficult and with modern methods of biopsy, dark field examination, and so forth, there should be little or no chance of error. The greatest danger lies in those cases where the carcinoma is limited to the depth of the lesion and thus missed in the biopsy speciman.

Accepted modalities of treatment are (1) surgery and (2) radiation. Radiation is subdivided into roentgen and radium therapy, each of which is again subdivided. End results obtained by all forms of treatment are reported.

In the treatment of cervical metastases, end results favor block dissection of the neck. External irradiation alone was shown to be insufficient to control such extension.

Eighty-six of 112 patients (77 per cent) are recorded as having a satisfactory end result, no case being omitted because of

extent of lesion. These individuals have been followed up for from two to sixteen years, averaging six plus years.

152 Clinton St.
Brooklyn 2, N. Y.

REFERENCES

1. Duffy, J. F. Indications for neck dissection and for irradiation of cervical nodes in intra oral carcinoma. In: Treatment of Cancer and Allied Diseases. G. T. Pack and E. M. Livingston, Editors. Paul B. Hoeber, Inc., 1940, Vol. I, pp. 557–594.
2. Howes, W. E. X-ray therapy of carcinoma of the lip and skin. *Radiology*, 1934, *23*, 71–74.
3. Howes, W. E., and LaRosa, F. J. Carcinoma of the lower lip. Am. J. Roentgenol. & Rad. Therapy, 1942, *47*, 39–49.
4. Howes, W. E., and Camiel, M. R. Contact roentgen therapy. Am. J. Roentgenol. & Rad. Therapy, 1942, *48*, 360–376.
5. Paterson, R., and Parker, H. M. Dosage system for gamma ray therapy. *Brit. J. Radiol.*, 1934, *7*, 592–632.
6. Paterson, R. Dosage in Radiation Therapy. Collected reprints from the Holt Radium Institute, Manchester, 1933–1941.

SURGICAL AND RADIATION TREATMENT OF CANCER OF THE BREAST*

By ROLF BULL ENGELSTAD, M.D.
OSLO, NORWAY

IN RADIATION therapy, as otherwise in medicine, empiricism has played a great part in the indications for its use, as well as in the working out of methods. The empirical method has undoubtedly in many fields been the obvious and necessary one and has often been fruitful. This also applies to radiation therapy in cancer, the development of which must necessarily be based on experience. The statistical evaluation of the treatment results has then offered some clues to the desirability of altering the methods.

For malignant growths, however, there is the disadvantage in the procedure that a great many years are required for the collection of usable and comparable statistics, if this is at all possible. In the meantime our material, based on knowledge and experience, has gradually become so extensive as to offer a fairly good basis for a logical construction of treatment methods.

In cancer of the breast a number of conditions, for example varying demands on the diagnosis, variations in classification of the material, difference in technique of the surgical as well as of the radiation treatment, and the different composition of the materials, join in making the statistics for the treatment results a difficult basis for continued work. Only exceedingly extensive and highly uniform statistics should permit the drawing of definite conclusions. The best, quickest and most certain road to an adequate treatment would, therefore, in my opinion, be the development of technique and methods on the basis of theoretical reasonings, using the available materials from anatomical, histopathological, tumorbiological, radiobiological, clinical and physical examinations.

Making reservations for the shortcomings of the statistics, a review will here be given of the treatment results in cancer of the breast obtained at the Norwegian Radium Hospital, and according to a procedure that has been used here for a number of years. First, however, the logical foundation for our methods will be briefly considered.

When first taking up these problems for discussion (at the annual meeting of "Norsk Kirurgisk Forening" in 1937) I raised the following questions, an answer to which is necessary for an evaluation of the importance of radiation treatment in cancer of the breast:

1. Is roentgen or radium irradiation as a supplement to surgical treatment likely to improve the obtainable results?
2. Can radiation treatment replace surgical operation?
3. Will an energetic preoperative irradiation permit a less radical surgical intervention?
4. What doses will secure the best possible effect?
5. Should radiation treatment be given preoperatively or postoperatively, or preoperatively and postoperatively, and according to which technique? Should roentgen or radium irradiation be used?

To the answer to these questions we hold some clues of fundamental importance, namely first of all our experiences regarding the radiosentitivity of the mammary carcinomas. The results from some of our investigations in this field have been published.[1] In 92 cases, preoperatively irradiated with epidermicide doses, the degree of the irradiation effect was studied in connection with histopathological examinations after radical operation, three to eight

[1] Engelstad, R. B. On treatment of carcinoma mammae. Experiences from Norwegian Radium Hospital. *Acta chir. Scandinav.*, 1942, *87*, 545–572.

* From the Norwegian Radium Hospital, Oslo, Norway. Chief: Rolf Bull Engelstad, M.D.

weeks after the preoperative treatment (Table 1).

Table I

	Cases
Complete destruction of tumor	17
Strong irradiation effect	40
Moderate irradiation effect	20
No or inconsiderable irradiation effect	15
	92

Seven of the 17 cases with complete destruction of the tumor had beforehand been histopathologically examined. The clinical picture of the 10 remaining cases left hardly any doubt as to the diagnosis of cancer.

The radiosensitivity of mammary carcinomas thus shows great variations. A great many cases are very favorably influenced by irradiation, but there are also radioresistant forms.

Neither do the lymph nodes react alike to irradiation. It is our definite impression, however, that radiosensitivity of these structures is less than that of the mammary tumor proper.

Some years ago we made some unsuccessful attempts to find a definite relation between the histopathological structure and radiosensitivity of the growth. Whether a classification or grading as used by Geschickter will prove able to give certain clues has not been tried in the present material. The examination, however, is at present an item of the hospital program.

In fact, our observations on radiosensitivity of mammary carcinomas, showing fair agreement with those of other investigations, actually offer a rather good basis for the answer to the first four of our questions.

Ad. 1. Considering the marked radiosensitivity of more than half the number of examined cases, it seems reasonable to presume radiation treatment in addition to surgical operation to be capable of improving the results.

Ad. 2 and 3. On the other hand, the rather considerable number of mammary carcinomas with slight radiosensitivity makes a limitation of the treatment to irradiation or to local removal of tumor plus irradiation seem hardly justified. In this connection, however, the remarkable results obtained by the Englishmen Keynes and McWhirter after such procedure should be recalled. There is every reason to follow continued work in this field with the greatest interest. Particularly valuable would be the finding of a more suitable histopathological classification than the one used today. Because of our personal experiences we do not yet feel justified in reducing the demands on the radical operation.

We therefore still maintain the routine method of radical operation plus radiation treatment.

Ad. 4. For the size of the doses we are calling on the same experiences and the same reasonings. To obtain the best effect in the greatest number of cases, the doses applied should be as large as possible without causing serious radiation injury.

Ad. 5. To answer the last of the questions, some more factors than those mentioned above should be considered. The object of the radiotherapeutic procedures is not merely injury to or destruction of the tumor cells in the mammary region and in the adjacent regional lymphatics. Decisive for the fate of the patient is practically always the distant metastases. An effort to prevent these formations should therefore be our main task.

This may seem hopeless, and if metastasis essentially happened hematogenously, so it would be. The great majority of investigations, however, point to the lymphatics as the main route for the spread of cancer of the breast ("lymphatic permeation," Sampson Handley), at least during the comparatively early stages of the disease.

In operable cases the surgical treatment —with more or less certainty—is capable of controlling the primary tumor and some of the lymphatics, namely the axillary, and at least some of the infraclavicular ones. But the supraclavicular, some of the deep fascial and the lymphatics on the inside of the chest wall are inaccessible to radical surgical therapy. Destruction of tumor cells along these lymph routes is the most important task of radiation therapy.

The areas to be irradiated are therefore, besides the mammary region and the axilla, also the infraclavicular fossa, the supracla-

vicular fossa, the deep fascial and the intrathoracic lymphatics. Most important are probably the latter. For the most effective and homogeneous irradiation of these regions, the operative removal beforehand of the breast with the underlying musculature and other soft parts is an essential advantage. This appears most convincingly from some figures which I have included in some of my earlier works. In my opinion anatomical, radiophysical, tumor-biological and radiobiological reasons favor the belief that *radiation treatment for cancer of the breast should be given postoperatively in one treatment series and with large doses.*

The most important advantages of the procedure may be summed up as follows:

(a) Conditions are rendered favorable for an homogeneous irradiation with the largest possible doses.

(b) Access is rendered easier to the very lymphatics that most need the radiation treatment, and that are inaccessible to surgical operation.

(c) Needless delay is avoided of the radical operation of a tumor that possibly is only slightly radiosensitive, or even entirely radioresistant.

The postoperative treatment may be given in the form of roentgen or radium irradiation. The roentgen treatment is given over two tangential fields covering the area from the anterior midline to the posterior axillary line, from the clavicle toward the costal arch in the mid clavicular line, including the mammary region, axilla and infraclavicular fossa (175 kv., 4 ma., filter 1 mm. Cu, focal skin distance 50 cm.). Daily doses of 350 to 400 roentgens and total doses of about 3,500 r per field are given. A large thorax may need a supplementary radiation field between the two tangential ones. In addition, a supraclavicular field is always irradiated. In radium treatment, the thoracic field with axilla and infraclavicular fossa is irradiated using a mold at a radium skin distance of 3 cm., and greatly protracted (application period six to seven days). Teleradium is then used over the supraclavicular fossa. In radium treatment, daily doses of 500 to 600 gamma roentgens and total doses of 3,500 to 4,000 gamma roentgens are used.

Satisfactory radiation penetration of the thoracic wall and of the other regions concerned are obtainable by both methods. But radium treatment, which we prefer for most cases, may offer certain advantages, such as a favorable distribution of the depth doses and continuous irradiation with low intensity over a comparatively long period of time. However, postoperative radium treatment of all mammary carcinomas is not possible with the disposable quantities of radium. If only for this reason must roentgen treatment be extensively used.

For inoperable tumors, primary radiation treatment is given. If the tumor thus becomes operable, a radical operation is done and this is followed by postoperative irradiation.

Cancer of the male breast is treated according to the same principles: radical operation and postoperative radiation treatment.

It stands to reason that a special institute for radiation treatment of cancer will admit a great many patients with recurrence or metastases, and who have earlier been treated at other hospitals. Such cases are seen to constitute a rather considerable part of the present material.

Local recurrences, cutaneous or subcutaneous nodules are treated with radium on a mold or roentgen therapy, occasionally with contact roentgen therapy. Freedom from symptoms, lasting up to more than ten years, has been obtained in a few cases.

Lymph node recurrences are treated with teleradium or roentgen therapy. Also here freedom from symptoms lasting for years may be obtained in rare cases.

Roentgen irradiation is used for skeletal metastases, often with singularly good palliative effects, and sometimes with striking improvement of the roentgenological changes.

As a rule, pulmonary and other visceral metastatses are not given radiation treatment.

Some years ago we tried total roentgen irradiation according to the method of Mallet in some cases of mammary carcinoma where there was a generalized extension; with no expectations, however, from a method that can hardly be thought especially effective except for the most highly radiosensitive tumors. Neither was there any effect worth mentioning. Therefore we have in late years not been using total irradiation for general metastases from carcinoma of the breast.

Some of the difficulties connected with an evaluation of the statistics of the treatment results for carcinoma of the breast have already been mentioned. The difficulties are so considerable that a comparison of different statistics will often be of very little value. When even so I have considered the publication of the material from the Norwegian Radium Hospital to have some interest, this is, for one thing, because the material has gradually become so extensive that some of the sources of error are sufficiently reduced to justify this statistical study. It will, at any rate, give a certain impression of the value and the deficiencies of the treatment methods employed. An analysis of the material, collated with other experiences, might also be thought capable of rendering some support to our efforts to improve the treatment.

The first difficulty to be faced, when working on cancer of the breast material, is the classification of the stages. One has to remain satisfied with a rather rough classification, based on the simplest possible clinical and pathologic-anatomical conditions that are capable of one interpretation only. Nevertheless, the border lines will be blurred and the classification often uncertain.

For a number of years we have been using the following classification:*

Stage I: Operable cancer of the breast with no clinically or histopathologically demonstrable spread.

Stage II: Operable cancer of the breast with clinically or histopathologically demonstrable operable metastases to the axillary lymph nodes.

Stage III: Inoperable cancer of the breast or inoperable axillary or infraclavicular metastases, or supraclavicular metastases (operable or inoperable).

Stage IV: Distant metastases (or recurrences).

Besides the erroneous sources of the classification, attributable to the inevitable presence of transitions, the ever existing possibility of uncertainty, due to imperfection of our examination methods, must be considered. Not the least difficult is classification of the individual patient in Stages I and II; this may even be impossible, especially in a large and inhomogeneous material like the present one. For some purposes the two stages will, therefore, for practical reasons, be regarded as one group.

In spite of all shortcomings, I believe our classification to be sufficiently simple to be practically applicable. It gives three large main groups:

The operable cases—with or without spread to the adjacent regional lymph nodes (Stages I and II).

The inoperable cases—inoperable either because of conditions in the primary tumor proper or in the adjacent regional lymph nodes, or because metastases have reached the lymphatics of regions that because of their location are inaccessible to radical surgery. In these cases, however, the condition is in a larger sense still regional (Stage III).

The incurable cases—in which spread has progressed beyond the regional lymphatics, forming distant metastases (Stage IV). Also recurrences in patients, who have earlier been treated elsewhere have, for practical reasons, been included in this group, although they actually belong outside the frame of a systematic stage classification.

The material here presented covers all patients treated—or examined—for cancer of the breast at the Norwegian Radium Hospital during the years 1932–1942. A

* The *clinical* demonstration of lymph node metastases has only relation to the cases where primary radical operation is not performed, as it is, of course, also necessary to classify these cases at the beginning of the treatment. In all cases primarily operated upon, i.e., *all* the patients who have received postoperative irradiation, the classification in stages is based upon *histopathological* examination of the lymph nodes.

total of *1,384 patients* have been treated here during this period; only those are included who have been observed for at least five years. Table II shows grouping of the material according to sex, civil position and number of children.

TABLE II

		Cases	Per Cent
Male		9	0.6
Female		1,375	99.4
of whom:	unmarried	394	
	married	981	
	number of children unknown	181	
	0 children	126	
	1 child	159	
	2 children	169	
	3–5 children	259	
	6 children or more	103	

I am content to record this distribution, and merely to deduce that the most varied categories are found well represented in the material: married and unmarried, women childless or with several children. Some time ago I had a statistician study these conditions compared to those in the normal population. The result of this evaluation was difficult to judge, but cancer of the breast seemed somewhat more frequent in women with few children than in those with a large number. At the same time, the cancer frequency within the various professions was investigated, but no statistically significant variations could be shown from one group to another.

The distribution of the ages is seen in Table III.

TABLE III

Under 30 years	11
30–39 years	141
40–49 years	391
50–59 years	382
60–69 years	299
Over 70 years	160
	1,384

The great majority of cases is found in the three decades from forty to sixty-nine years, and as many as 56 per cent in the forties and fifties. About 10 per cent is found as early as in the thirties, whereas before the age of thirty years the condition is very rare. This age distribution, which is fairly well known, may serve to illustrate the great social importance of mammary carcinoma.

It is a common belief that cancer of the breast is most frequently found in fat women. The present material indicates no tendency in this direction (Table IV), but definite conclusions cannot be drawn, as there is no material that can be used for comparison.

TABLE IV

	Cases	Per Cent
Corpulent	265	19.0
Normal figure	862	62.4
Thin	257	18.6

The histories have been studied with a view to other information concerning the patients' physique and appearance, whether they have been strikingly feminine or more masculine types, but no usable clues have been found.

In Table V some information from the histories has been recorded.

TABLE V

	Cases
Earlier mastitis	36
Earlier adenofibrosis	37
Menstrual disturbances	41
Pregnancy, lactation	24
Trauma	50

As is seen, a history of mastitis, adenofibrosis, menstrual disturbance or trauma is not very frequent, at least not as frequent as to be considered of special importance in connection with the question of the etiology. The 24 cases occurring, or being shown, during pregnancy or lactation will be discussed at a later point.

Distribution of the material into the various stages (Table VI) will evidently not

TABLE VI

	Cases	Per Cent	
Stage I	278	20.1	55.8%
Stage II	494	35.7	
Stage III	182	13.1	
Stage IV	430	31.1	

be the same from a radiotherapeutic institute as from a general surgical department.

Stages I, II and III are seen to make up 68.9 per cent, Stages I and II, 55.8 per cent of the total material. As these groups are the most interesting to us, they will be especially discussed in the following.

The fact that as many as 31.1 per cent are found in Stage IV is in itself not surprising, considering that these patients can be treated radiologically only, and therefore are referred to us. In this group there are some patients with distant metastases—to the skeletal system, to the lungs and other internal organs. Of these the skeletal metastases are well suited for palliative roentgen treatment, whereas the others, as a rule, are intractable. There are some patients with recurrences (or metastases) after earlier treatment at other institutes. These are local recurrences, often readily influenced, and in which freedom from symptoms years long in duration is not rarely obtained, lymph node recurrences or metastases which can be influenced to some extent, and recurrences (or metastases) to the skeletal system, to the lungs and to other internal organs, with the possibilities for treatment described above.

Especially during the first years of the Hospital's activities was the number of advanced cases (Stages III and IV) comparatively very large. This condition has gradually become somewhat altered, partly because the lack of accommodation has made us refuse many hopeless cases. There is the possibility, however, that a different cause—namely, more attention on part of the patients and the physicians—is partly responsible for this change in late years in the direction of the earlier stages. This would be a result of the educational work that has been concentrated on cancer of the breast more than on any other form of the disease.

Up to 1934 inclusive there were more patients in Stage IV than in Stages I and II together, but conditions have steadily improved. In 1938 and 1939 the number of patients in Stage I alone about equalled that in Stage IV, and the following years have shown more patients in Stage I than in Stage IV. There is no chance of this change being the result of an altered evaluation of the stages on our part, as Stage IV is an absolutely clear cut and well defined group, which, in contrast to the other stages, allows no fluid transitions. Only cases showing recurrence or distant metastases are registered as Stage IV.

It might be of interest to find out whether the distribution to the different stages bears some relation to the age at which the disease occurs (Table VII).

TABLE VII

PERCENTAGE DISTRIBUTION TO STAGES

	I	II	III	IV
Under 30 years	45.5	45.5		9.0
30–39 years	17.0	42.6	8.5	39.9
40–49 years	22.3	37.6	11.3	28.8
50–59 years	19.9	33.7	13.4	33.0
60–69 years	17.4	35.8	13.7	33.1
Over 70 years	21.3	28.8	21.3	28.6

The number in the age group below thirty years is too small to be included. Stage II shows comparatively few cases from the oldest age group; that, on the other hand, is noticeably well represented in Stage III. Less attention on part of the aged may possibly be partly responsible for this. Stage IV has its greatest percentage contribution in the age group thirty to thirty-nine years, which possibly may have some connection with the often very rapid spread seen in young patients. On the other hand, many chance conditions will certainly make themselves especially felt in Stage IV.

Next the treatment methods employed will be considered (Table VIII).

Stages I and II are joined into one group, having been treated according to the same principles.

Radical operation followed by postoperative irradiation has been used in the great majority of cases in Stages I and II. The fairly extensive use of other methods, as

seen from Table VIII, is due partly to the deficient development of our present treatment methods during the first years of our activities, partly to the fact that we have not always been free in the choice of treatment; that has been decided by dispositions already made before the admission to the

TABLE VIII

	Stages I–II	Stage III	Stage IV
Non-radical operation	3	1	
Non-radical operation plus irradiation	41	10	4
Radical operation	3	2	1
Radical operation plus preoperative irradiation	36	23	
Radical operation plus pre- and postoperative irradiation	18	16	
Radical operation plus postoperative irradiation	609	61	10
Irradiation only	20	38	317
No or incomplete treatment	42	31	98

Norwegian Radium Hospital. In Stage III are seen a number of cases of amputation of the breast with axillary dissection. These are partly inoperable tumors that have become operable subsequent to radiation treatment, partly supraclavicular metastases where these have been thought capable of being controlled by irradiation, and partly where the method has been thought capable of giving the best possible palliative effect and prolongation of life. The latter arguments also apply to most patients in Stage IV in whom radical operation has been done in spite of the presence of distant metastases.

The postoperative control examinations of these patients have, in the great majority of cases, been made by ourselves, where difficulties of geographical or other nature have not been too great. In the latter and in a few other cases the control examination has been made at the hospital of the patient's home district, where she has usually also been operated on, or by the patient's own physician. Observation of the patient has, as a rule, been continued beyond the usual period of five years. In every case contact with the patient has been kept up by some means.

This control system has proved very effective. Of the 1,384 cases only 7 patients have been lost track of.

Six hundred and ninety-eight patients have an observation period of ten years (Table IX).

TABLE IX

	Total		Symptom Free		Per Cent	
Stage I	100	330	59	138	59.0	41.8
Stage II	230		79		34.4	
Stage III	91		3		3.3	
Stage IV	277		8		2.9	

Table IX does not require extensive comments. It shows a ten year symptom-free period in 41.8 per cent of the cases in Stages I and II together. Some patients who have died from intercurrent disease and without signs of recurrence of the cancer have not been included, so that the correct percentage of recoveries actually is somewhat higher.

The nearly 3 per cent of symptom-free cases in Stage IV may seem surprising. All of these patients, however, have been treated for local recurrence. In no case with distant metastases has ten years, or even five years, of freedom from symptoms been obtained.

The mammary cancer was bilateral in 44 patients, in most cases with a shorter or longer interval of time between manifestation of the cancer in the two breasts. Of these there were 8, that is 18.6 per cent, symptom free after ten years.

No patient in the present material has been observed for less than five years, and the results will be studied somewhat more closely. A review of the results after five years of observation is found in Table X.

The four stages seen collectively show 520 of 1,377 cases to be symptom free after five years, that is *37.8 per cent.* There is no

Table X

	Total	Symptom Free 5 Years	Per Cent
Stage I	274	220	80.3
Stage II	494	261	52.8
Stage III	181	17	9.4
Stage IV	428	22	5.1

reason, however, why patients belonging in Stage IV should be included in this general review, partly because the condition in these patients has become generalized, partly because they have been treated elsewhere at some earlier point of time, and have come to the Radium Hospital with recurrences to receive palliative treatment, or merely because they have wished something to be done. It is remarkable nevertheless that five years of freedom from symptoms has been obtained in 5.1 per cent of these hopeless cases. The great majority of these is made up from patients with local recurrence; in a few cases there are lymph node recurrences in the axilla or supraclavicular fossa.

tion will be given of the five year results for the total material (Table XI).

In view of the fact that many patients in the present material are of an advanced age, it stands to reason that some have died from intercurrent disease in course of the observation time. A really correct picture of the value of the treatment methods applied would require a correction for the symptom-free patients who have died from intercurrent disease. In some cases, however, an estimation may be difficult or information unsatisfactory, and I have therefore desisted from correcting the results to a calculated freedom from symptoms, and shall merely state that the percentage numbers recorded undoubtedly are somewhat low.

The presence in the five year material of 65 cases (47 per cent) in the different stages of *bilateral* manifestations should also be mentioned. Twenty-one of these, or *32.3 per cent, are symptom free.*

In Table XII are seen the results after five years of observation for Stages I and II collectively. The material consists of 768 patients.

Table XI

	Stage I	Stage II	Stage III	Stage IV
Symptom free	220 (80.3%)	261 (52.8%)	17 (9.4%)	22 (5.1%)
Symptom free, died from intercurrent disease	20	38	8	5
Alive with recurrence	1	13	6	15
Died from breast cancer	33	182	150	386

Study of the total result for Stages I, II and III gives 498 symptom-free cases after five years of observation in a material of 949 patients, that is *52.5 per cent* of operable and inoperable cases. Most interest, however, centers on Stages I and II, the operable cases, because only here can one speak of a radical radiological-surgical treatment, and because only these two stages are capable of offering comparable statistics.

Before proceeding in our study of Stages I and II, however, more accurate informa-

The present material, in comparison with the one which I published in 1942, shows further improvement. In 1942 there

Table XII

	Number	Per Cent
Symptom free	481	62.6
Symptom free, died from intercurrent disease	58	7.6
Alive with recurrence	14	1.8
Died from breast cancer	215	28.0

was freedom from symptoms after five years in 77.4 per cent of the cases in Stage I, in 46.8 per cent in Stage II, and for stages I and II collectively the result was 54.4 per cent. Possibly the larger numbers, and therefore the more reliable statistics may be held partly responsible for the apparent improvement. It should be permissible, however, to think that the continued development and systematizing of the treatment methods has also played a part.

To find out whether age is of any importance in the prognosis, in Table XIII the results for Stages I and II have been arranged according to age.

TABLE XIII

Age	Total	Symptom Free	Per Cent
Under 30 years	10	5	50.0
30–39 years	84	53	63.1
40–49 years	234	171	73.1
50–59 years	203	117	57.6
60–69 years	157	90	57.3
Over 70 years	80	45	56.2

The age group under thirty years shows the lowest percentage number of symptom-free cases; however, the number is too small for conclusions to be drawn. The result for the group thirty to thirty-nine years is more favorable than for any group over fifty years, but poorer than for the group forty to forty-nine years; this ranks highest of all with 73.1 per cent. Therefore the material does not indicate a particularly bad prognosis for the relatively young. On the contrary, the results are apparently poorest in the older ages.

The results should also be studied in relation to the different treatment methods employed. This comparison must be limited to Stages I and II, the smaller groups being left out (Table XIV).

The highest percentage of symptom-free cases is found among the postoperatively irradiated cases, whereas the two other groups are too small to justify a comparison.

The routine treatment method at the Norwegian Radium Hospital, namely teleradium treatment of the supraclavicular fossa and radium on a mold over the mammary field with axilla and infraclavicular fossa, has already been given. In Table XV these patients have been separated from those treated with roentgen therapy, and also the ones operated on and postoperatively treated at the Norwegian Radium Hospital have been placed in a separate group. In the present material this latter group is still very small, but it has grown considerably in the following years. However, as yet the observation time is too short.

TABLE XIV

	Total	Symptom Free	Per Cent
Radical operation plus preoperative irradiation	36	20	55.6
Radical operation plus pre- and postoperative irradiation	18	12	66.7
Radical operation plus postoperative irradiation	609	420	69.0

TABLE XV

POSTOPERATIVELY TREATED, STAGES I AND II

	Total	Symptom Free	Per Cent
Norwegian Radium Hospital routine method	448	320	71.4
Operated and postoperatively irradiated at Norwegian Radium Hospital	22	19	86.4
Roentgen treated	139	73	52.5

Of the 22 patients, operated upon and postoperatively treated at the Norwegian Radium Hospital, 19 (86.4 per cent) are symptom free after five years. As mentioned, however, the number is too small to be statistically significant. But also our impressions in late years tell of somewhat more favorable results in these cases. I have no intention to suggest that this, if true, would be attributable to our surgical tech-

nique. But the early institution in these conditions of postoperative radiation treatment, four to five days after the operation, may play some part. And there is good reason for assuming this to be an important point.

Table xv further shows better results to be obtained after our postoperative radium treatment than after roentgen irradiation. Not attaching too much importance to these figures, I still believe them to be the expression of a certain real difference. It should be mentioned in this connection that the radium-treated patients are, by no means, a selection of favorable cases. The amount of radium at our disposal at the hospital is not sufficient for radium on a mold for all patients who need it, and roentgen irradiation has therefore to be used for some. The rule is, then, that patients in Stage II are given priority in treatment with radium, as in these cases the treatment is considered most urgently needed. When there is not enough radium for all, roentgen treatment is therefore first of all given to patients in Stage I.

As mentioned above, a rather extensive use of roentgen radiation for postoperative treatment is unavoidable. The quantities of radium required for treatment of all cases would far exceed the amount in this country today. Too much importance must naturally not be attributed to the figures given here. When evaluating the treatment results for cancer of the breast the erroneous sources are many and incalculable.

The question must now be asked: Is there any good reason why radium treatment should give better results than roentgen irradiation, considering that the biological effects of the two kinds of rays are identical? The answer will be that, at least with the methods used today, the conditions for radium treatment are possibly more favorable. The distribution of depth doses is very helpful, and—what is possibly even more important—continuous irradiation with radium, with low intensity over a period of six to seven days may, according to the present knowledge of the importance of the time factor to the biological radiation effect, well be thought to yield somewhat more than the fractionated or protracted-fractionated roentgen irradiation.

It would, in my opinion, be a mistake to neglect the indicated difference in treatment results of the two forms of postoperative irradiation. The consequence of this must be an attempt to modify the technique of roentgen irradiation so that this will approach as nearly as practically possible the conditions of radium treatment. For this purpose we have tried partly a reduction of the radiation intensity, but first and foremost a more fractionated irradiation, with two daily seances, permitting a somewhat larger daily dose. As soon as the results had become clear to us, we changed the postoperative roentgen treatment of cancer of the breast at the Norwegian Radium Hospital, in an effort thus to improve the results.

Before leaving the statistical discussion of our material, a special group of mammary cancers, namely those occurring in connection with pregnancy or lactation, should be mentioned. It is probably a general experience that cancer of the breast in these conditions is particularly malignant, possibly because of the change in hormonal conditions. The considerable difficulty of recognizing a tumor in a lactating breast may be partly responsible. It is important in these cases that the breast should be emptied of milk before the examination. By this means an otherwise impalpable tumor may be felt.

The present material includes 24 cases of cancer of the breast during pregnancy and lactation. The distribution to the different stages and the results after five years of observation are seen in Table xvi.

Earlier our impression has been that the prognosis in these cases was hopeless, but this is apparently wrong. A decisive factor heretofore has possibly been the often late institution of treatment in these cases because of the diagnostic difficulties. Making reservation for the small number in this part of the material, the chances for recovery in the early stages (Stages I and II) do not seem essentially different from what

is to be expected in the other forms of the disease. In any case, it should be permissible to regard the prognosis as not hopeless.

During the period covering this material no other method than operation and radiation treatment has been used by us to any extent worth mentioning. We have thus only lately and to very small extent tried the effect of hormones on mammary cancer.

TABLE XVI

	Total	Symptom Free	Per Cent
Stage I	4	4	
Stage II	9	6	
Stage III	2	0	
Stage IV	9	0	
All stages	24	10	41.6

Preclimateric castration of patients with cancer of the breast has for a long time had its adherents. This has been based partly on animal experiments (Lacassagne *et al.*), partly on experience of the greater malignancy of mammary cancer during pregnancy and lactation. Formerly we have very rarely used this method, and then only for otherwise intractable metastases or recurrences. We have not earlier used castration as part of the routine treatment. The most marked effect observed up to now, as far as I have been able to find out, has been limited chiefly to cases with distant metastases, especially to the bony skeleton. Although animal experiments may have proved castration at a young age capable of preventing mammary cancer, this does not mean that castration at an advanced age would have the same effect on the fully developed cancer. The value of castration as part of the routine combined treatment of cancer of the breast has not been convincing. It is therefore natural that a treatment so strongly affecting the lives of women will be regarded with some reserve.

Lately, however, another method has been added, necessitating a revision of this view, namely the experiences of the effect of the androgenous hormone. Up to now the method has been tried here in no more than 11 cases, with daily injections of 100 mg. of testosterone propionate (Testin Nyco) up to total doses of 2,500–4,000 mg. Our material consists of 3 patients with local recurrence, and with convincing result in no case; 4 patients with metastases to the spine, with some relief from pain in 2, but with objective improvement in none; and 3 patients with metastases to the lungs, showing distinct reduction of the metastases in one, no change in the second, and continued progression in the third, and finally one patient with supraclavicular lymph node recurrence in whom questionable temporary improvement was seen. At present we have some other patients receiving the treatment, but it is too early to judge the effect.

Our personal results are thus very modest, but some cases have been recorded (among others by Adair and Prudente), one has also been demonstrated to me, in which striking effect had been obtained, even if merely temporary. It can therefore hardly be doubted that treatment with the androgenous hormone in large doses *may* have some influence on the condition, at least on some of its manifestations.

Collating all experimental and clinical observations, it seems most probable that the sexual hormones play some, possibly a great part in the occurrence and further development of mammary cancer, and that the influence on the hormonal balance may be used therapeutically.

We have therefore thought it appropriate to make these problems a subject of investigation. At present the work is pending in collaboration with Knud Nicolaysen, Jens Bjørneboe and Per Laland. The procedure today at the Norwegian Radium Hospital is the following:

For Stage I the usual radiation and surgical treatment is used, as a rule not in connection with any form of hormonal therapy.

Also for Stage II the radiation and surgi-

cal treatment is unchanged, but here it is combined with ovarian roentgen irradiation with doses of 1,200–1,500 roentgens (measured on the skin) over each of two (or three) fields, followed by testosterone propionate 100 mg., three times a week for ten weeks. During the treatment period the urine is regularly examined for androgenous hormone.

For Stage III the same combined radiation and surgical treatment is given as before, adapted to the special conditions of the individual case, and in addition the ovaries are irradiated and testosterone propionate injections given in some cases.

Stage IV is usually treated with irradiation over the ovaries and possibly with testosterone. Roentgen irradiation is used as before for skeletal metastases, and roentgen or radium treatment for local recurrences, as for recurrences or metastases to lymph nodes, whereas metastases to the lungs and other visceral organs, as before, are given local irradiation in exceptional cases only.

The doses used for irradiation of the ovaries are considerably larger than the usual roentgen castration doses. It has lately been claimed by several authors that producing menopause is not enough. It is believed that a stronger influence on the ovarian hormone production is required. For the same reason irradiation of the ovaries is used also after the climacterium. Otherwise there are no clues to the determination of the optimal roentgen dose for the ovaries; possibly they should be even larger than those used today.

The development of a severe and stubborn leukopenia sometimes makes the combination of postoperative radiation treatment and irradiation of the ovaries difficult to accomplish. Therefore the advantage of an operative castration may be considered. Temporarily we are trying to gain the point by reducing the size of the fields for ovarian irradiation as much as possible, in every case marking off projection of the ovaries on the abdomen and on the back.

It is still too early to form an opinion of the possibility for making use of the discoveries in late years in the field of atomic physics in the treatment of cancer of the breast. This applies to neutrons, positrons and fast electrons alike. The latter might be thought capable of offering certain advantages, if they can be emitted from the apparatus in sufficient amounts and in a wide enough beam. Neither is applicability of the radioactive isotopes very well known. Were isotopes with long half-life period and with sufficient intensity of the gamma rays available, these might perhaps enable a more extensive use of postoperative radiation treatment, according to the method that has for a long time been used at the Norwegian Radium Hospital. Another question, and still more important, is what can be obtained by an internal selective irradiation, that is the peroral or parenteral use of isotopes with short radiation period and with special affinities, conditioning a deposition in the tumor cells or in the tumor-infiltrated organs and tissues.

Finally, it should be mentioned that in cancer of the breast attempts have been made to use the radioactive isotopes for diagnostic purposes, here also taking advantage of a special affinitity for the tumor cells.

A sound scientific evaluation of the various new methods that are being or will be tried in the years to come, will probably require a number of years. Although it might be permissible to expect great results from some of these methods, there is no reason today why our present irradiation and surgical methods should not be continued. The development in recent years of the combined radiation and surgical treatment has been seen to bring about a noticeable improvement in the results. Continued development in this field, combined with the efforts to enable an early diagnosis, will undoubtedly lead to further improvement of the results for this exceedingly important form of cancer.

Norwegian Radium Hospital
Oslo, Norway

COMPLICATIONS FOLLOWING THE USE OF LOW INTENSITY, LONG RADIUM ELEMENT NEEDLES IN THE TREATMENT OF CANCER OF THE CERVIX UTERI*

By G. W. WATERMAN, M.D., *and* E. M. TRACY, M.D.
PROVIDENCE, RHODE ISLAND

IN SEVERAL articles published since 1930[5,6,11,12] we have described and illustrated a method of treating cancer of the cervix with long element needles. Survival rates both five and ten years have been given and complications reported briefly. It is the intention in this paper to discuss complications in more detail in order to dispel certain naturally occurring fears as to the propriety of placing these long needles deep into the pelvic structures. Severe infections, peritonitis, parametritis, frequent fistula formations, injuries to bladder, ureters and intestines have been foreseen and warned against. That this has not been our experience, as we hope to show, we attribute to the type of needle used and to the wide distribution of these weak sources by which we have attained a more uniform irradiation of high total dosage.

A study of the natural course of carcinoma of the cervix reveals that its spread into the pelvic structures is by two routes (Fig. 1): (1) primarily by direct infiltration into the paracervical and parametrial

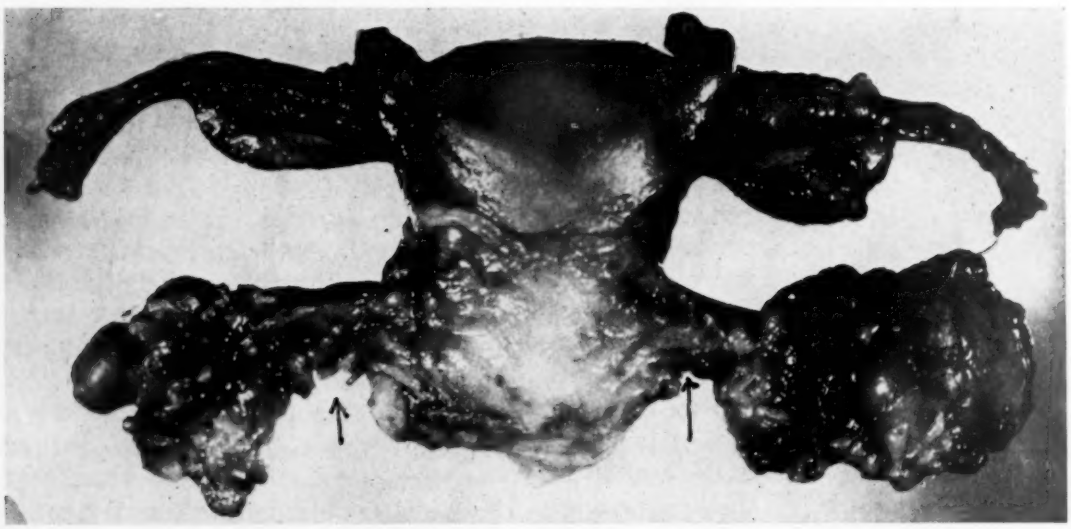

FIG. 1. This photograph of the authors' hysterectomy specimen is shown to illustrate the mechanism by which ureteral obstruction occurs. Note direct invasion of parametrium from the cervix and secondary invasion or growing-in of carcinoma from hypogastric and obturator nodes. Most ureteral obstructions are the result of carcinomatous invasion and are not of radiation origin. Specimen was removed from patient whose cervical cancer had been treated transvaginally with roentgen irradiation with superficial healing.

* From the Tumor Clinic, Rhode Island Hospital, Gynecological Service, Providence, Rhode Island. Presented at the Forty-eighth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 16–19, 1947.

structures and adjacent viscera, (2) secondarily by lymphatic metastasis to pelvic nodes followed by invasion beyond their walls into surrounding tissue spaces with final growing back towards the cervix and complete parametrial fixation when the outward and inward masses join. The ureters may be caught in either form of extension. Their walls may be invaded and narrowed, and obstruction occur. The bladder base is invaded anteriorly and the rectum posteriorly. When, by the natural course of the disease, ulceration occurs with necrosis and crater formation, fistula is the natural termination. When cancer of the cervix in the more advanced forms is treated with radium, it is often difficult to say whether the fistulous complication or ureteral obstruction occurred as the result of the disease or the radium treatment. It is really only in the early case where the fistula comes immediately following treatment and where the cancer is controlled that responsibility can be justly determined. The injuries caused by radium and roentgen rays through their destructive action on the normal tissues have been well described in the literature[1,2,3,7,8,9] and need no further elaboration in this paper.

MATERIAL FOR STUDY

This study is based on the clinical records of 621 patients seen and examined at the Tumor Clinic of the Rhode Island Hospital 1926–1941. Of this number 95 were too advanced to treat, received their initial treatment elsewhere, or were treated with roentgen radiation for palliation only. Thirty-seven were treated by other methods than needles, leaving a total of 489 cases where needles were used as the primary planned treatment, 77 per cent of all the cases. (Many of the cases not treated with needles came in the earlier years when we were experimenting and had not yet adopted the needles as routine.)

Table I

Year	Stage	Needles	Roentgen Treatment	Time	Cause of death
1927	III	+	o	9 days	Embolism
1928	III	+	o	14 days	Nephrosis toxic (autopsy)
1928	IV	+	o	25 days	Hemorrhage
1930	IV	+	o	30 min.	Collapse—after anesthesia
1931	III	+	o	32 days	Sepsis—thrombophlebitis
1931	IV	+	+	21 days	Pyelonephritis (autopsy)
1932	III	+	o	16 days	Pyelitis—peritonitis
1932	IV	+	o	3 days	Embolism
1935	III	+	o	33 days	Peritonitis
1936	III	o	+	30 days	Pyelitis—*B. coli*
1937	III	+	+	22 days	Hemorrhage
1937	IV	+	+	14 days	Pelvic cellulitis; peritonitis

FOLLOW-UP

As our follow-up through our secretary and social worker has been very efficient and as practically all our patients are Rhode Island residents—a small state—we feel that our records are quite complete with only 2 cases lost (a follow-up of 99.7 per cent).

COMPLICATIONS

The following complications have been selected for discussion: (1) immediate mortality; (2) fistula formation; (3) urinary complications; (4) intestinal complications; (5) severe inflammatory reactions.

Immediate Mortality. By immediate mortality we mean death occurring during hospital stay following treatment (Table 1).

A review of these deaths shows a gross mortality for the 621 cases absolute of 12 of 621, or 2 per cent, or for the cases treated with radium needles, 11 out of 489, or 2.2 per cent. All of these deaths were in advanced cases in anemic, debilitated, and often septic states. All occurred before 1938. The 2 deaths due to embolism certainly are not directly attributable to the method. The 2 deaths from hemorrhage might conceivably be but as they both occurred some time after the radium needles were removed, it is doubtful that the needles were the cause. The 1 postanesthesia collapse death is not due to the needles. Three cases of death from kidney sepsis or nephrosis surely represent poor preoperative study and preparation rather than a fault of the needles. The 3 cases of peritonitis or cellulitis resulting in death (0.6 per cent of treated cases) occurred before we had any sulfa drugs or antibiotics for combatting such conditions. The fact that we have had no immediate mortality from 1937 through 1946, except 1 case of embolism who died on the ninth day, in 394 cases treated would seem to indicate that needles are not directly responsible or should not be responsible for immediate mortality if cases are carefully studied as to blood status and kidney function, with intravenous pyelography, etc., and if possible sources of sepsis are cleared up either by preliminary roentgen therapy or by use of the sulfa drugs and penicillin before treatment.

TABLE II

SUMMARY

Embolism	2
Toxic nephrosis	1
Hemorrhage	2
Collapse	1
Sepsis thrombophlebitis	1
Sepsis pyelitis or pyelonephritis	2
Peritonitis or cellulitis	3:489 or 0.6%

Fistula Formation. Breakdown of tissues in the vaginal tract resulting in fistulous openings into the bladder, rectum, and small intestine can occur as the result of over-irradiation. They also occur spontaneously, as has been pointed out, during the later or more advanced stages of the disease where the cancer is uncontrolled by treatment. It is difficult, therefore, to place the blame for the fistula occurring late or as a terminal condition where active cancer is present. Fistulas are sometimes present before treatment or in the group having initial treatment elsewhere. Also it would seem that we should distinguish between the fistula occurring after primary treatment and that occurring after re-treatment. A high percentage of fistulas occurring after primary planned treatment would certainly be a serious objection to any method whereas one should expect a certain greater morbidity after re-treatment for uncontrolled cancer by any method. Table III gives the fistula incidence.

TABLE III

CASES OF FISTULA

1926–1941	621 cases (absolute)
Total number of fistulas—	56 (9.0%)
Present on admission 6	
Initial treatment elsewhere 8	
Treated primarily at Rhode Island Hospital	42
Total cases treated (all methods)	549
Fistula—all methods	42 (7.7%)
Treated with needles—primarily	489
Fistulas in primarily needle treated cases	40 (8.2%)

In order to show the time relation of the fistulas, whether after primary planned treatment, or after re-treatment, Table IV is presented.

Where radium needles alone were used as the primary treatment in 258 cases, no fistulas occurred in Stages I and II and for all stages the incidence was 3.1 per cent. Of the 77 re-treated cases, 8, or 10.4 per cent, developed fistulas, showing the increased liability to such damage following re-treatment. There seems to be a decided increase in fistula incidence when a combination of interstitial needles and external roentgen irradiation is used, the incidence rising from 3.1 per cent to 6.1 per cent in the primary group and from 10.4 per cent to 18.5 per cent in the re-treated group.

This study seems to confirm our impression of many years that external roentgen irradiation must be used with caution where interstitial radium treatment is contemplated.

One ileovaginal fistula occurred in a stump case. The patient died of peritonitis following an operation for repair of the fistula. Another ileovaginal fistula not shown in Table v occurred in a patient who had had a complete vaginal hysterectomy elsewhere for cancer of the cervix, was retreated for recurrence with needles, developed an ileovaginal fistula which was successfully closed by intestinal resection and anastomosis. The vesico-utero-colic fistula occurred in a patient who had a large growth invading the fundus. A departure from the usual technique in that a 50 mg. capsule filtered by 0.5 mm. of silver and 1 mm. of brass was placed in the fundus and by some mistake left in place forty-two hours instead of twenty-four hours resulted in a massive breakdown of the fundus with fistula from colon to bladder.

Table IV

FISTULA FORMATION

(A) Primary treatment—Radium Needles Alone 1926–1941

	No. of Cases	Fistulas	No. of Cases Re-treated	Fistulas
Stage I	18	0—0	3	0 0
Stage II	96	0—0	31	3—9.7%
Stage III	107	5—4.7%	37	5—13.5%
Stage IV	37	3—8.1%	6	0—0
Totals	258	8—3.1%	77	8—10.4%

(B) Primary treatment—Radium Needles plus Roentgen Therapy

Stage I	4	0—0	0	0—0
Stage II	65	5—7.7%	12	2—16%
Stage III	125	5—4.0%	35	5—14%
Stage IV	37	4—10.8%	7	3—43%
Totals	231	14— 6.1%	54	10—18.5%
Grand Total	489	224—.5%	131	18—13.7%

Table V

TYPES OF FISTULAS ENCOUNTERED—489 CASES

Vesicovaginal	16—3.2%
Rectovaginal	11—2.2%
Both vesicovaginal and rectovaginal	11—2.2%
Ileovaginal fistula	1 stump case
*Ileovaginal fistula—primary vaginal hysterectomy elsewhere vaginal vault recurrence	1
Vesico-utero-colic	1
Total	40

* Not included in total; re-treated case—after surgery for cancer elsewhere.

Table VI shows the outcome of 40 cases treated with radium needles developing fistulas.

Table VI

Died with fistula—cancer uncontrolled	21
Closed spontaneously	6
Closed surgically	5
Died following repair	4
Living with fistulas 5 yr. or more	4
Total	40

Urinary Complications—Not Fistulas. Irradiation changes based essentially on an endarteritis or sclerosis resulting in ischemic edema and fibrous replacement or, if severe, in necrosis occur in varying degrees. The early or first degree injury results in some dysuria and frequency, often with mild hematuria. On cystoscopy after a few months the mucosa appears pale and shiny with loss of mucosal markings. Numerous small telangiectatic vessels and an occasional small ulceration appear. This lesion is often non-progressive although attacks of hematuria may recur over many years. We have 7 such cases on record. It is interesting to note that this lesion appeared most often in the Stages I and II and usually (5 of 7 cases) where extensive roentgen irradiation was used. A more severe reaction with actual ulceration, a sort of second degree lesion, is also observed. Here the findings are those of extensive bullous edema with

ulceration and incrustation, and occasionally stone formation, often leading to an erroneous diagnosis of cancer. These are serious lesions, are apt to bleed dangerously and the hemorrhage is difficult to control. In 1 of our 4 cases in our earlier experience, we were led by gross appearance to implant further radium needles intravesically. When the pathological report reached us several days later, the radium was withdrawn. After considerable suffering and many hospitalizations, this patient is still alive and without cancer, but with her right kidney removed and a nephrostomy tube in her left kidney. It will be eighteen years since her original treatment. A cystectomy and transplantation of ureters was necessary to control bleeding in another case. A patient with a lesser degree of ulceration survives nine years with only an occasional slight hematuria. A fourth case died of extensive pelvic spread of cancer. It is questionable if her lesion was irradiation reaction or was due to carcinomatous invasion.

Obstruction of the ureters due to irradiation and not cancer has occurred in this series in 8 cases. In deciding whether the ureteral stenosis was due to irradiation and not cancer we have had some difficulties: for example, in 1 case the patient, a large Stage II adenocarcinoma with pyometra developed a left hydronephrosis about three months following treatment, the hydronephrosis being demonstrated by an intravenous pyelogram. She had been treated with needles plus roentgen irradiation externally. As no preliminary pyelogram had been done, we do not know just when the hydronephrosis developed. Death from cancer five months after treatment, and two months after the hydronephrosis was discovered, makes it difficult to say whether this case should be included. It certainly is unusual in our experience to have hydronephrosis develop so early after treatment. In another case a large ulceration of the trigone associated with nodules along the urethra was re-treated with radium needles plus roentgen irradiation one year after primary treatment for Stage III carcinoma of the cervix. A cystoscopy two years later showed hydronephrosis. She survived for eight years after the primary—seven years after re-treatment—finally died of cancer. With these 2 cases included, we have 8 cases of hydronephrosis and hydroureter due to radiation injury—8 of 489 cases, or 1.6 per cent. We now have adopted the practice of routinely doing pyelograms on all but the early cases.

TABLE VII

URINARY COMPLICATIONS OTHER THAN FISTULAS

Hematuria	7
Ulcer of bladder	4
Obstruction of ureter with hydronephrosis or pyonephrosis (due to treatment)	8
Total	19—3%

Intestinal Complications—Not Fistulas. Although fortunately not frequent, intestinal complications when they occur are much to be dreaded. Mild proctitis is often encountered, especially with the added use of deep roentgen therapy. Usually this is not of long duration but when persistent and accompanied by a bloody or mucous discharge, it should be watched with care as an early symptom of the development from serious lesions. These mild complications have not been included in this study.

Rectal ulceration usually occurs back of the vaginal fornix or cervix and is usually accompanied by a hardening and thickening about the circumference of the bowel resulting in an annular ring or constriction with parametrial and perirectal fixation. This gives the impression of recurring cancer and has often led to more treatment with roentgen radiation, to the patient's detriment. In 1 case (1932) we did a radical resection of uterus and rectum for such a lesion to find that the rectum contained no cancer but an irradiation reaction. The uterus did contain uncontrolled adenocarcinoma which seemed to justify our procedure. We have had 10 cases of severe rectal or sigmoidal ulcers in this series, the last, an incidental autopsy finding,

occurring in 1937; 10 of 489 or 2 per cent. Three cases of small bowel ulceration and stenosis were all associated with stump cases, the ileum being adherent and damaged by the radium or perhaps the radium broke down cancer-invaded intestinal wall.

There were 2 cases of ulcer of the rectosigmoid which perforated with resulting peritonitis and death. This accident occurred four months after radium treatment and six months after roentgen irradiation in the first case, and nine months after radium and three months after roentgen irradiation in the second. The first had operation with findings of perforation and peritonitis; an autopsy established the diagnosis in the second case. We have 1 case of necrosis and perforation of the transverse colon, remarkable because we were able to get her into the hospital and repair her intestine in time to save her life. This perforation occurred three months after roentgen irradiation and two months after radium treatment. She later developed both rectovaginal and vesicovaginal fistulas. The rectovaginal fistula closed spontaneously and after several years we successfully closed the vesicovaginal fistula. She is now alive and well, free of disease nine years after her original treatment.

TABLE VIII

SUMMARY OF INTESTINAL COMPLICATIONS

Ulceration and obstruction of small bowel	3
Ulceration of rectum and sigmoid	10
Perforation of sigmoid	2
Perforation of transverse colon	1
Total (fistulas not included)	16, or 3.3%
Rectovaginal fistulas in needle treated cases	22, or 4.4%
Total severe intestinal injuries in 489 needle treated cases	38, or 7.7%

Severe Inflammation. A careful search of our records shows that severe inflammatory reactions have not been a frequent accompaniment of treatment by this type of interstitial needle. As we have never withheld treatment because of low grade temperature, or made it our practice to remove needles in the course of treatment for slight rises, we think that our low incidence of severe inflammatory reactions is significant.

TABLE IX

SEVERE INFLAMMATORY REACTIONS

The following cases of severe inflammatory reaction were found:

Pyometrium	2
Retroperitoneal abscess	1
Pelvic inflammatory disease	3
Total	6 or 1.2%

Severe Inflamation—6 cases in 489—1.2 per cent

1. Pyrometrium—2 cases
   (1932) One case Stage III—1932—developed pyometrium requiring dilatation and drainage three months after treatment with roentgen radiation and needles. The cancer was not controlled and she died within one year.
   (1933) A second case—Stage III—required dilatation and drainage five months after treatment. She lived fourteen years but died of massive pelvic recurrence with spinal metastases.
2. Retroperitoneal abscess—1 case
   (1933) One case—Stage III—developed retroperitoneal abscess described as on right side between liver and transverse colon—required drainage through right rectus incision. Now alive and well after fourteen years.
3. Pelvic inflammatory disease—3 cases.
   (1934) 1. Pelvic abscess—Stage IV—drained abdominally ten days after treatment. Died three months later of cancer.
   (1933) 2. Acute pelvic inflammatory disease—Stage III—high temperature for several weeks after treatment. Had roentgen irradiation and radium at same time. Roentgen irradiation 3/8 to 4/26/33, radium 3/10 to 3/17/33. This patient died seven and one-half years later of a massive recurrence of cancer.
   3. Pelvic inflammatory disease—Stage II—also in 1933. Roentgen irradiation and radium given at the same time. Roentgen irradiation 7/21 to 8/23/33. Radium 7/29 to 8/4/33. Had very very severe flare

up which subsided in two weeks. Required surgery for residual inflammatory masses in tube and ovaries and for peri-appendicitis five months later. Now alive and well without recurrence fourteen years.

SUMMARY

The authors have reviewed a series of 621 cases of cancer of the cervix—1926 to 1941. Four hundred and eighty-nine of these were treated primarily by interstitial irradiation with the long radium element needles. Complications of immediate mortality, fistula formation, urinary and intestinal lesions—not fistulas—and severe inflammatory pelvic reactions have been described as they occurred in this clinic.

The incidence of these complications has not exceeded in general that reported by other clinics using other methods.[1,2,3,4,7,9,10]

CONCLUSIONS

Interstitial irradiation by the long radium element needles has been relatively a safe method in our experience and has not been followed by a high incidence of complications.*

G. W. Waterman, M.D.
155 Thayer St.
Providence, Rhode Island.

REFERENCES

1. ALDRIDGE, A. H. Intestinal injuries resulting from irradiation treatment of uterine carcinoma. *Am. J. Obst. & Gynec.*, 1942, *44*, 833–857.
2. CORSCADEN, J. A., KASABACH, H. H., and LENZ, M. Intestinal injuries after radium and roentgen treatment of carcinoma of cervix. AM. J. ROENTGENOL. & RAD. THERAPY, 1938, *39*, 871–887.
3. MARTIN, C. L. Elimination of irradiation injuries in the treatment of cancer of the cervix. AM. J. ROENTGENOL. & RAD. THERAPY, 1943, *49*, 494–503.
4. MEIGS, J. V. Discussion of paper by Aldridge.[1]
5. PITTS, H. C., and WATERMAN, G. W. Treatment of cancer of cervix uteri at the Rhode Island Hospital. *Surg., Gynec. & Obst.*, 1937, *64*, 30–38.
6. PITTS, H. C., and WATERMAN, G. W. Further report on radium treatment of carcinoma of cervix uteri. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *43*, 567–576.
7. TOD, MARGARET C. Optimum dosage in treatment of carcinoma of uterine cervix by radiation. *Brit. J. Radiol.*, 1941, *14*, 23–29.
8. TOD, MARGARET C., and MEREDITH, W. J. Dosage system for use in treatment of cancer of uterine cervix. *Brit. J. Radiol.*, 1938, *11*, 809–823.
9. TODD, T. F. Rectal ulceration following irradiation treatment of carcinoma of cervix uteri. *Surg., Gynec. & Obst.*, 1938, 67, 617–631.
10. WARD, G. G. Diagnosis and treatment of carcinoma of corpus uteri based on experiences at Woman's Hospital. *Am. J. Obst. & Gynec.*, 1942, *44*, 303–309.
11. WATERMAN, G. W., and DILEONE, R. Treatment of carcinoma of cervix by interstitial radium needles at Rhode Island Hospital. *Am. J. Obst. & Gynec.*, 1945, *50*, 482–488.
12. WATERMAN, G. W., DILEONE, R., and TRACY, E. Use of long interstitial radium needles in treatment of cancer of the cervix. AM. J. ROENTGENOL. & RAD. THERAPY, 1947, *57*, 671–678

* For discussion see page 797.

Vol. 60, No. 6

POSTIRRADIATION ULCERATIONS OF THE UTERINE CERVIX*

By HAROLD W. JACOX, M.D.
NEW YORK, NEW YORK

LATE postirradiation complications involving the bladder and rectum in cases of carcinoma of the cervix are now recognized and frequently anticipated. These complications generally occur months or years after radiation therapy and are caused by occlusive vascular changes. Some difficulty is experienced from time to time in differentiating the postirradiation complications, in the form of necroses or ulcerations, from recurrences or extensions of carcinomatous growths.

Similar postirradiation ulcerations caused by vascular occlusions occurring in the cervix itself would cause considerable diagnostic difficulty.

Four such cases were encountered occurring in a three year period among 99 patients with cervical carcinoma treated with roentgen and radium therapy in the Tumor Clinic of The Western Pennsylvania Hospital in Pittsburgh.

CASE REPORTS

CASE I. A colored woman, aged thirty-six, weighing 114 pounds , with a vaginal discharge for three months, had a fleshy, friable mass 3 cm. in diameter in the cervix involving mostly the anterior lip. It was classified as a League of Nations Stage II. Microscopically, this tumor showed all degrees of differentiation, but was predominantly Grade 3, on a basis of Grade 4 being the most undifferentiated.

High voltage roentgen treatments with 200 kv. and 0.5 mm. Cu filtration were given over a period of twenty days and consisted of 1,800 roentgens (measured in air) to each of four areas 10 by 15 cm. in size over the lower part of the abdomen and the sacrogluteal regions. This was applied at the rate of 150 to 200 r to each of two portals daily, except Sunday, alternating front and back. The estimated tumor dose was 2,380 r. Two weeks later radium was inserted for thirty hours. A total of 3,000 milligram-hours was administered. A 50 mg. radium capsule filtered with 1 mm. of platinum was placed in the cervical canal, and four 10 mg. radium needles each 2 cm. long and filtered with 0.5 mm. of platinum were inserted in the parametrium, and one 10 mg. needle into the anterior cervical lip. It was estimated that the posterior fornix received about 7,500 gamma roentgens; the anterior cervical lip about 9,700 gamma roentgens and the parametrium 2,850 gamma roentgens, all measured on a plane at the end of the active length of the radium. A biopsy of the cervix just prior to the radium therapy showed no evidence of neoplasm.

The cervical lesion healed completely. However, seven months later the vaginal vault presented a crater 4 cm. in diameter. The edges of the crater were indurated and the lesion was considered neoplastic. Microscopically, however, no evidence of neoplasm was seen.

At the end of the following month additional biopsies were performed on the cervix and crater. These also failed to show any evidence of neoplasm. There was extensive hyaline necrosis with associated panarteritis, phlebitis and thrombosis.

Two months later several small radiation ulcers were noted in the bladder wall. The cervix was improved and fleshy granulation tissue was present.

During the following year the patient failed to report. She was symptom free and had gained weight.

Two years after radiation therapy, partial intestinal obstruction developed and at laparotomy extensive peritoneal metastases were proved histopathologically, but the cervix and adnexa were free of disease. The patient died of abdominal carcinomatosis one month later.

CASE II. A colored woman, aged thirty-four, weighing 115 pounds, had vaginal bleeding for two months. The cervix was fixed and the parametrium was infiltrated—a Stage III. Friable, neoplastic tissue was present in the cervical canal. Biopsy showed a Grade 3 squamous cell carcinoma. Roentgen treatment, with a total

* Presented at the Forty-Eighth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 16–19, 1947.

of 1,600 r in air to each of four portals about the pelvis with an estimated tumor dose of 2,120 r, was given in a period of three weeks. This was immediately followed by the insertion of radium, two 50 mg. capsules in tandem in the uterus and cervix and four 10 mg. needles into the parametrium, for twenty-four hours, or 3,360 mg-hr. The radium dosage in gamma roentgens was only slightly greater than in the first case; that is, 8,000 in paracervical tissues, 9,000 in cervix, and 3,000 gamma roentgens in the parametrium.

One month later there was improvement, but at the end of another three months a small raised area was noted at the site of the posterior cervical lip. Microscopically, this showed extensive hyaline necrosis of vessels associated with diffuse necrosis of tissues and leukocytic infiltration, but no evidence of neoplasm.

This lesion improved for a short time, but then deteriorated, so that eight months later a large slough was removed from the region of the cervix. Under the microscope this tissue showed hyaline necrosis and thrombosis of large and small vessels. No tumor cells were present.

Another large slough was removed from the same site one month later, leaving a rectovaginal fistula. The rectovaginal fistula healed, but a vesicovaginal fistula formed. Later this was successfully repaired and the cervix was absent. Seven years after the radiation therapy there was no evidence of tumor recurrence or metastases.

CASE III. A colored woman, aged thirty, weighing 124 pounds, with vaginal bleeding of six months' duration, and a recent profuse hemorrhage had an ulcerative and proliferative lesion at the external cervical os which proved to be a Grade 3 squamous cell carcinoma histopathologically, and Stage III clinically.

Over a three week period, 1,550 r was given to each of two anterior pelvic and 1,450 r to each of two posterior pelvic portals with an estimated tumor dosage of 2,000 r. No microscopic evidence of neoplasm was found one week after completion of these treatments. Following the biopsy, one 100 mg. tandem of radium was inserted into the uterine and cervical canals and four 10 mg. needles were placed around the circumference of the cervix. These remained in place for twenty-eight hours or a total of 3,920 mg-hr.

Seven months later the vagina was greatly contracted and there was hard, nodular and partially necrotic tissue, which did not bleed readily, in the vaginal wall. The posterior lip of the cervix was also hard and nodular. Microscopic examination of these tissues showed no evidence of neoplasm.

One month later, two additional biopsies were made of the cervix and vagina because of the resemblance of these lesions to carcinoma. There was, again, no evidence of neoplasm, but severe radiation changes with many occluded vessels were present.

A vesicovaginal fistula developed which gradually improved over a period of eighteen months. The patient is living with urinary incontinence, but without evidence of neoplasm seven years after the radiation therapy.

CASE IV. A colored woman, aged twenty-nine, weighing 110 pounds, had been spotting for three weeks. There was a large fungating mass in the cervix which was friable and bled easily, a League of Nations Stage II. Sections showed a Grade 3 squamous cell carcinoma. Roentgen treatments were given over a period of twenty-three days and consisted of 1,550 r to each anterior pelvic region and 1,750 r to each sacrogluteal region for a tumor dose of 2,310 r. Radium was then inserted for twenty-four hours; two 50 mg. tubes into the fundus and cervix and five 10 mg. needles radially into the paracervical tissues for a total of 3,600 mg-hr.

Check-up examination seven months later showed the radiation reaction had subsided. The cervix was healed and clean; the uterus movable and the parametrium free. The patient had gained weight.

During the following month rectal bleeding developed, and at the end of the month a crater was found in the vaginal vault. This had a gray base and an indurated, red border which was suggestive of recurrent malignancy. However, under the microscope, no evidence of neoplasm was seen.

Additional changes in the vaginal vault, which suggested recurrent tumor and which prompted biopsies, were noted two, three, seven and eight months later, a total of 5 biopsies negative for neoplasm within one year. None of these showed any evidence of tumor cells.

The patient was well seven and one-half years after radiation therapy. There was no evidence of recurrence. The vaginal lesion remained healed. The patient had gained 65 pounds and had no complaints.

DISCUSSION

In each of these cases lesions developed at or near the site of the original cervical carcinoma which suggested a recurrence of the malignant growth. In one of these the impression was so strong that, pending the report of the biopsy, a hopeless prognosis was considered.

In the sections of the lesions from each of these cases the classical vascular occlusive changes secondary to irradiation were demonstrable. These vascular changes caused infarction with the associated necrosis and ulceration. Treatment consisted simply of daily boric acid vaginal douches.

We were impressed by the fact that all our cases occurred in young, thin, colored women and the ulcerations developed approximately eight months after treatment when the radiation reaction had subsided.

Equal or larger amounts of irradiation with a similar technique were received by other patients, both colored and white, during the same period without the development of this complication. It is believed that the vascular apparatus of some individuals is more vulnerable than others or that the ability to form scar tissue is greater in some patients. None of this group had serology positive for syphilis.

Only by microscopic examination of tissues from the suspected lesions was their true nature established, and additional damage was avoided by withholding further radiation treatments.

622 West 168th St.
New York 32, N. Y.

REFERENCES

1. Jacox, H. W., Johnston, J. R., and Gross, P. Noncarcinomatous postirradiation ulcerations of cervix. *Pennsylvania M. J.*, 1942, *46*, 119–121.

DISCUSSION OF SYMPOSIUM ON CANCER OF THE UTERINE CERVIX*

Dr. James A. Corscaden, New York. It is indeed a great privilege to be invited to discuss these important gynecological papers—important because cancer of the cervix is second in frequency only to cancer of the breast; and second, because no matter how desirous one might be to operate on all cancer, by the surgeon's own statement only 15 per cent are eligible, leaving 85 per cent of this very common disease needing roentgen rays and radium for their therapy.

The chronicity of Dr. Jacox' cases I think is typical and should warn us against secondary irradiation after apparently adequate irradiation has already been given. The longest interval in my experience between irradiation and the vesicovaginal fistula is twenty-two years. Almost anything could have caused that fistula in that long interval. It raises in my mind the question of the wisdom of giving these secondary treatments. In our experience, the results do not warrant the risk.

In looking over these accidents, there seem to be two groups of causes: the uncontrollable, and those which may be controlled. I have been more interested in trying to study those factors which might help us avoid the injuries, and first is the time factor. In Dr. Jacox' cases the radium was given in from twenty-four to thirty hours and the roentgen radiation in from twenty days to four weeks. I want to illustrate these questions by some experiences of our own.

(Slide) This is a slide of 2 patients, both very similar in complexion, and so forth, and superficially comparable. I wish to point out that among all these factors, the essential difference between the 2 cases is the duration of the treatment. The first woman received 6,400 r in eighteen days. The other woman received 9,000 r in forty-five days. The first woman died with ulceration of the skin, perforation of the intestine; the other was perfectly well, with practically no symptoms whatever.

The next slide expresses the same idea in radium. Up to about 1937 we used to give 175 mg. for forty hours, and in those cases there were 10 per cent of clinically important injuries—the late injuries, not the discomforts experienced during treatment. We changed to 70 mg. for 100 hours, giving the same total, and there have been none of these late complications.

The next question I would like to ask is, how far were the bladder and intestine from the radium units as applied? (Slide) This is a diagrammatic drawing, drawn so that the distance from intestine to radium in the upper dia-

* Papers by Drs. Waterman and Tracy, and Jacox.

gram is half the distance of that in the lower. Obviously, the intestine close to the radium would receive four times the dose the bowel would in the other. In the roentgen treatment, that is pretty well calculated in most cases, but because of the difficulties of measurement in radium, it is almost always omitted in the expression of dosage.

Turning to Dr. Waterman's cases, I think, first, we should thank him for such a frank and clear presentation of his accidents; and second, compliment him on the low incidence. The vagueness of the area into which these needles are plunged makes one apprehensive that they may be entering bowel, bladder, or ureter, and I think it is important to see that his fistulas, among the cases that have been cured of cancer, are very small in number. I cannot get interested in fistulas accompanied by cancer. There are so many variables that we have nothing to calculate upon. I think we should concentrate upon the so-called cured case that does have fistula, and in his series the number was very small.

The question comes up in his cases whether the distribution of the radium might have had some effect on the results. The next slide shows the typical intracavity irradiation by various techniques where occasionally the radium is crowded into the uterus and fornices. Five or six thousand milligram-hours given in forty-eight hours would be a heavy dose. Given in a week 7,000 or 8,000 mg-hr. would be very high and close to the danger point.

This slide shows the pelvis peppered with radium needles, and the next slide diagrammatically shows the radium scattered throughout the pelvis. This, in total, is a little over 100 mg. for 120 hours, giving 12,000 milligram-hours without injury because the needles each contain a small amount of radium and are widely dispersed. In calculating dosage the disposition of the radium must always be taken into account.

The next slide confirms Dr. Waterman's emphasis on the necessity of calculating the radium plus the roentgen-ray dosage, at any particular point. The vast majority of intestinal lesions occur in the rectosigmoid, not exactly where the maximum amount of radium was, caused by the combined action of roentgen rays and radium.

Finally, I would like to show another slide to take the action of the irradiation on the intestine out of the mystery class. It seems to me that the intestinal mucosa is specifically susceptible, and this slide shows that. This is the patient who died from over-irradiation. I would like to point out that there is very little reaction in the peritoneum. The muscularis is pretty much intact, although the irradiation came from outside, but the intestinal mucosa is badly disintegrated. In other words, the radiation dosage should be expressed in terms of what the intestinal mucosa will bear rather than in tumor doses, because this actually is what limits the amount of irradiation which we are able to give.

DR. ARTHUR W. ERSKINE, Cedar Rapids, Iowa. The conclusions of Drs. Waterman and Tracy and Dr. Jacox agree fairly well with those published by Watson, Herger and Sauer in the June, 1947, number of the *Journal of Urology*. It seems that we can expect serious irradiation injuries in at least 3 per cent of the patients who live three or four years after being treated skillfully, carefully and adequately for pelvic malignancies. There must be at least three reasons for the increasing number of reports of such reactions: (1) radiation therapists are using larger, and more nearly adequate dosage; (2) we are looking for reactions, and as both essayists have pointed out, are less likely to mistake them for recurrences; (3) more patients are recovering. It is obvious that if 50 patients out of 100 live five years, more reactions will be seen than if only 25 survive.

Reports, such as these, might tempt the faint hearted to avoid radiation sequelae and other unpleasant complications by refraining from using adequate dosage. The only point I wish to make is that no such inference can properly be drawn. We know these essayists and we know that their patients were treated carefully and skillfully. In spite of that care and skill some patients developed unpleasant, painful, and dangerous reactions. Those reactions should have the same significance as operative deaths. The nature of our calling demands that we have a certain amount of fortitude. We deal with human life and with a cruel, insidious, deadly disease. If we treat our patients with that disease fairly, if we are doctors, we shall accept a definite morbidity and mortality rate just as surgeons and all good doctors do.

DR. G. E. PFAHLER, Philadelphia, Pa. I would like to ask a question of Dr. Waterman as to the size and length of the needles, the quantity

of radium content, and some details about his technique of application.

Dr. Charles M. Richards, San Jose, Calif. I have been very much interested in these presentations, particularly that of Dr. Jacox, because, as all of us know who have been in this work for a good many years, we have these things come up, and it is not very pleasant, after you have seen a case of cervical cancer in the office or in the hospital month after month, staying perfectly well, to have the patient appear all of a sudden with a large ulcer.

There are certain things that we notice that enable us, I think, to make a clinical diagnosis and therefore allay our fears, even without biopsy of this particular ulcer. My experience is that these things are definitely not hyperplastic in character. They are obviously and characteristically decadent in character.

The question comes up as to what to do. I note that Dr. Jacox says his patients have been cured of the radium necrosis of the cervix with just boric acid irrigations. We have found very helpful the use of some of the nitrogen products, such as allantoin and urea products combined with some local sulfathiazole application, and a packing every other day with an ointment of this material followed by irrigation the second day with 1–5,000 potassium permanganate solution. We have found this treatment very helpful in clearing up these radiation necroses.

One or two other ideas come to mind as to the distribution of the time of the irradiation. In many quarters it seems that the time interval between the deep roentgen therapy and the local radium application, whichever one comes first, is an important factor in allowing a certain amount of recovery of the normal tissues from the unavoidable exposure to irradiation. The recent tendency has been to increase the time between radium application and roentgen-ray application in order to allow this recovery of normal tissue.

Another very important point which was brought out many years ago, I think by Dr. Healy at Memorial Hospital, is the necessity of watching the direction of our primary beam in irradiating the pelvis with deep roentgen therapy to avoid central concentration of the beam into the area where local radium has been applied.

Dr. U. V. Portmann, Cleveland, Ohio. I would like to call attention to a complication that may result from radiation therapy for cancer of the cervix which has not been mentioned by the essayists. Several years ago there was a report from the Cleveland Clinic about patients having symptoms, signs, and roentgenologic evidence of obstruction of the small intestine who had had radiation therapy for cancer of the cervix a year or more previously. At operation a segment of the small intestine was fibrosed, and after removal recovery was uneventful. At first the surgeon who had used the radium attributed the condition to roentgen therapy until it was pointed out that one of these patients had not been so treated.

The symptoms of obstruction might be erroneously attributed to extension of the malignant disease. Possibly patients who were thought to have died of carcinoma have actually died of this condition. When a woman who has had radiation therapy for carcinoma of the cervix complains of symptoms of intestinal obstruction, even several years after treatment, she should have a roentgenologic gastrointestinal examination. The condition can be readily recognized, and resection of the affected segment is indicated.

Dr. Waterman (closing). I should like to answer Dr. Pfahler, and to say that these needles are long needles; the 3 mg. needles are 60 mm. long and the 2 mg. needles 45 mm. The entire detail of these instruments was very carefully described in the article which I read before the American Radium Society last year, and which was published in the July, 1947, issue of the American Journal of Roentgenology and Radium Therapy. I should be very glad to forward a reprint of that article to Dr. Pfahler if he would like to have one.

Dr. Jacox (closing). I had no axe to grind in presenting this paper, because I would like to know what caused this complication. Dr. Corscaden didn't answer it. Other people both white and colored, were treated during the same time, and a five year survival rate of 33 per cent of all cases was established during this same time. So, just why these individuals were susceptible, I don't know.

I have been looking for this in a white woman. We had one where we thought that was the case. We had a number of negative biopsies—that is, negative for cancer—but that woman eventually died of what we considered clinically distant metastases. The local area cleared up. Unfortunately, we did not get an autopsy or operative specimen as we did in the first case.

I don't know what the reason for this ulceration is. Maybe we overtreated them. There must have been something wrong, or the fact that these people just could not take it. I do not know how to pick them out in advance. If anyone has any suggestions, I would like to hear them.

The point that Dr. Richards brought up is most important, I believe: the time interval between the roentgen-ray series and the insertion of the radium. As you all know, if you wait too long you will have closure of the cervical canal and you cannot get the radium in. My thought is to hit the cancer as hard and as fast as you can and you will get a small percentage of these troubles, as Dr. Erskine stated.

It did not seem to make much difference what we put on these ulcerations. You see the trouble goes back of all that. You can put all kinds of things on the surface of the ulcer and if you do not get what is down underneath it out of the way—which in this case happened to be the thrombosed, obliterated end arteries and all the changes I mentioned—all you can do with the surface is keep it clean, and if it will heal it will heal by collateral circulation. I believe that is the fundamental thing.

If I may, I should like to say something about what Dr. Waterman mentioned in these early cases. He did not say why he thought he got bladder complications in some of them. That is a distressing thing, to get bladder ulceration or hematuria in an early case, we will say in a Grade 1 or Grade 2, and I think it has a lot to do with the cancer acting as a filter, and when you have a small amount of cancer and you give the same dose that you give when you have a large amount, then you do not have the cancer acting as an absorbing structure to take up the radiation and be eliminated if the cancer disappears. That is one explanation. It may not be all, but if anyone has any suggestions or ideas about this, I would be glad to hear from him afterwards.

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TREATMENT OF CANCER OF THE PENIS AT THE NORWEGIAN RADIUM HOSPITAL*

By ROLF BULL ENGELSTAD, M.D.

OSLO, NORWAY

STUDY of the literature on the treatment of cancer of the penis indeed reveals a very extensive use of radiation treatment, as a rule, however, combined with preceding more or less radical surgical interventions. In a work from Radiumhemmet, Stockholm, Hansson[1] recommends amputation of the penis followed by radiation treatment for the great majority of cases. Radiation treatment alone will, in his opinion, essentially come into consideration for local irradiation (contact or interstitial application) of small superficial tumors, and for some advanced cases with inoperable glandular metastases, where amputation of the penis for palliative purposes is not considered safe. Metastases to the lymph nodes are first irradiated and, if necessary, followed by dissection of the inguinal glands.

The rather unsatisfactory results of radiation treatment alone from Radiumhemmet as from many other tumor clinics are, according to Hansson, attributable to several unfavorable factors. First, these tumors are highly differentiated spinocellular carcinomas with comparatively slight radiosensitivity. Second, infection of the phimotic prepuce is a frequent complication. Third, the prepuce and glans are apt to develop a radionecrosis.

As opposed to the routine of many other clinics, primary radiation treatment of cancer of the penis has been much used at the Norwegian Radium Hospital.

The usual procedure here has been first to perform a phimotic operation of some kind, and follow this by radium treatment of the penis tumor, using partly teleradium with doses of about 500 gamma roentgens a day, partly radium on a cylindrical wax mold (two halves of a cylinder), with a radium skin distance of 0.7 cm. (on rare occasions 1.5 cm.), and with daily doses of 500–700 gamma roentgens. As a rule, the total dose has been 3,500–3,700 gamma roentgens, occasionally about 4,000 gamma roentgens. For persistent tumor or for recurrence, the main rule is amputation of the penis. If the patient has already been operated upon at another hospital and arrives with or without recurrence radiation treatment is given, usually in the form of teleradium over the penis stump and the groins.

Roughly, the same methods are used for treatment of the glandular regions as for many other malignant tumors, beginning with radiation treatment, usually teleradium with doses of 3,500–4,000 gamma roentgens, whether or not metastases are demonstrable. For persistent glandular metastases dissection of the groins is done after six to eight weeks. The same treatment is also used for later occurring metastases to the glands. A disadvantage of the procedure, however, is that on really radical dissection of the groins subsequent to irradiation with large doses, necrosis of the skin is apt to develop, considerably delaying the course, and it may also lead to the formation of massive scar tissue, interfering with an effective control examination of this region during the further course.

The procedure that I had an opportunity to see at Radiumhemmet some time ago—namely, dissection of the groins to remove a fair section of the irradiated skin, sewing edges of the wound to the underlying layers, and covering the defect with skin graft—eliminates or reduces the above mentioned disadvantages, and therefore it seems an essential improvement upon the surgical methods. Also at this hospital the

[1] Hansson, C. J. Cancer of penis and its treatment. *Acta radiol.*, 1938, *19*, 443–457.

* From the Norwegian Radium Hospital, Oslo, Norway. Chief: Rolf Bull Engelstad, M.D.

procedure has been used in a few cases.

For treatment of the penis carcinoma proper we have, as mentioned, in the majority of cases used primary radiation treatment. As will be seen in the following, amputation of the penis has often been necessary at some later time, because of persistence or recurrence of the tumor. In these cases, however, a less radical amputation has been considered permissible. A limited electrocoagulation instead of amputation has been considered sufficient in a few cases.

We have wished to present our material on cancer of the penis, not because of any essential difference between our results regarding lasting freedom from symptoms, and those of others, but because the material, on account of the treatment methods employed, may possibly contribute to the illumination of the problem of the radiosensitivity of these tumors.

In course of the years 1932–1942 inclusive, 72 histopathologically verified cases of carcinoma of the penis have been treated, while during the same period we have, in male patients, had 601 cutaneous carcinomas, 473 labial carcinomas and 16 anal carcinomas, thus making a total of 1,162 carcinomas of the skin and in the areas around the natural openings of the body. In the present material carcinoma of the penis is thus not a frequent form of tumor, constituting no more than 6.2 per cent of the total number of the above mentioned growths. During the same period we have had 144 cases of carcinoma of the vulva.

Distribution as to age is seen in Table 1.

TABLE I

	Cases
30–39 years	3
40–49 years	13
50–59 years	15
60–69 years	22
70–79 years	11
80–89 years	8
	72

Manifestation of the condition before the age of forty is apparently rare, and the largest number of cases in our material is found in the fifties and sixties.

Phimosis, luetic infection and trauma have been mentioned as etiological factors. In fact, lues as well as a history of earlier trauma has been given by some of our patients, but the material allows no conclusions to be drawn as to the importance of these conditions. The presence of phimosis is fairly frequent, being found in 50 of 72 patients, that is in 69.4 per cent.

The importance of phimosis as a predisposing factor in the development of carcinoma of the penis is so well known that further discussion of the condition is unnecessary here. Only the prophylactic importance of treating every case of phimosis will be emphasized. It is true that very few patients with phimosis do develop carcinoma of the penis. But an early instituted treatment of the condition will, besides having a cancer prophylactic effect, also save the patient several, if less serious troubles, such as acute, recurrent and chronic balanitis, and the sometimes rather considerable pain on coitus. In my opinion an operation is important not only in the presence of complete phimosis, but also in incomplete cases, as also in the latter cases the condition may easily lead to deficient cleanliness.

When cancer develops in a patient with phimosis, we make a point of starting the treatment with a phimosis operation, preferably extirpation of the prepuce. If this cannot be done, at least a slit is made. This practically always facilitates the accomplishment of the radiation treatment, and also allows a more effective control of the condition during its further course.

Thirty-four of our 50 patients with phimosis were operated upon for the condition. In the 16 remaining cases there were either various obstacles in the way of an operation (adhesion of prepuce and glans, extensive tumor infiltration of prepuce and glans), or the prepuce or the entire foremost part of penis had been destroyed, or amputation of the penis had already been performed before admission.

For classification of our cases of cancer of the penis we have used Berven's method, based on condition of the lymph node metastases, with the difference, however, that Stage I has been divided into two subgroups.

Stage I: Without demonstrable metastases to the lymph nodes.
(Stage Ia.: Maximal diameter of penis carcinoma $\leqq 2$ cm.
Stage Ib.: Maximal diameter of penis carcinoma $\geqq 2$ cm.)
Stage II: Clinically demonstrable metastases to the lymph nodes, confined to the lymph nodes proper. Operable.
Stage III: Metastases to the lymph nodes with signs of perforation of the capsule. Inoperable.

The classification by stages thus is based on the clinical diagnosis of metastases to the lymph nodes and their operability, in both of which conditions an estimation may be difficult. The clinical determination of whether or not the enlargement of a gland is attributable to metastases may sometimes be easy, at other times exceedingly difficult or impossible. In Stage II therefore have been included only cases in which size and consistency of the glands make the diagnosis of cancer fairly certain. Also the question of operability of the case may be difficult to decide. On a whole, however, a classification on these principles is feasible and fairly definite.

The present material shows the following distribution to the various stages (Table II):

TABLE II

Stage I		36 (50%)
Ia	15	
Ib	21	
Stage II		28 (38.9%)
Stage III		8 (11.1%)

We shall at once proceed to study the total results, regardless of the treatment methods employed. Table III gives the patients who are alive and symptom free after three and five years respectively. The diagnosis has in all cases been histopathologically verified.

TABLE III

	3 Years		5 Years	
	Total	Symptom free	Total	Symptom free
Stage I	36	32 (88.9%)	27	24 (88.9%)
Stage Ia	15	14 (93.3%)	11	11 (100 %)
Stage Ib	21	18 (85.7%)	16	13 (81.3%)
Stage II	28	19 (67.9%)	22	14 (63.6%)
Stage III	8	0	8	0
	72	51 (70.8%)	57	38 (66.7%)

TABLE IV

STAGE I

	Total	Symptom Free	Died from Cancer	Died from Intercurrent Disease
Radiation treatment	20	18	1	1 (3 yr.)
Radiation treatment plus electrocoagulation	4	3	1	
Radiation plus surgical treatment	10	10		
Surgical plus radiation treatment	1	0	1	
Surgical treatment	1	1		
	36	32	3	1

I will not dwell at length on these results, which although apparently somewhat better than those usually seen, still are found roughly to be about the same. There is reason to point out the singularly favorable

prognosis for early cancers of the penis without metastases to the lymph nodes, the considerably poorer, if still relatively good prospects for Stage II, and the bad prognosis where inoperable metastases are found.

Considerably more interesting in this connection is trying to obtain some impression as to the effect of the radiation treatment. The results for Stage I (Ia and Ib collectively) have therefore been grouped according to the treatment methods employed (Table IV).

The corresponding results for Stage II are found in Table V.

The 8 patients belonging in Stage III were all far advanced cases with regard to development of the primary tumor and metastases. Six of these received only radiation treatment, whereas 2 had been operated on beforehand, and on admission had inoperable glandular recurrence, 1 also had recurrence of the primary tumor. One of these was treated with radiation, whereas the second one was considered intractable. All 8 patients died from cancer.

To study the course of the development also in the patients who died may have some interest. Table VI gives the causes of death; that is, to the best of my judgment I have attempted a characterization of the development that appeared mainly responsible for the fatal outcome.

Of patients dead of Stage Ia only 1 showed progression of the primary tumor. This patient had been operated on earlier, and arrived at this hospital with local recurrence without metastases to the glands. Here he received radiation treatment only. For the rest the table shows progression of metastases to the glands, alone or associated with progression of the primary tumor, to be the main cause of death in most cases.

In the two tables presenting the results of the different treatment methods (Tables IV and V), the treatment, as a whole, of the condition has been considered; that is, treatment of the primary tumor and of the metastases to the glands. The principles of our treatment of metastases to the glands have already been stated and will not be further discussed. It will merely be pointed out that the regional lymphatics are always irradiated, whether or not they are suspected, and also the importance stressed

TABLE V

STAGE II

	Total	Symptom Free	Died from Cancer	Died from Intercurrent Disease
Radiation treatment	10	7	2	1 (2 yr.)
Radiation treatment plus electrocoagulation	1	1		
Radiation plus surgical treatment	13	8	5	
Surgerical plus radiation treatment	3	3		
Surgical treatment	1	0	1	
	28	19	8	1

TABLE VI

	Stage Ia	Stage Ib	Stage I	Stage II	Stage III
Intercurrent disease		1	1	1	
Progression of the primary tumor	1		1	1	1
Progression of the glandular metastases		1	1	2	4
Progression of the primary tumor and glandular metastases		1	1	3	3
Distant metastases				2	
	1	3	4	9	8

of not delaying dissection of the groins, if after preceding irradiation there are found persistent, newly formed or recurrent metastases.

Finally, an analysis will be attempted of the data in the material regarding effect of the radium treatment upon the primary tumor proper, in order to gain an impression of the radiosensitivity of cancer of the penis. It is evident that interest in this connection is centered on the patients receiving primary radiation treatment with or without subsequent surgical operation, to the exclusion of primary operated and later irradiated cases (Table VII).

Table VII

	Total	Primary Radiation Treatment			Dead	
		Radiation treatment only	Later electro-coagulation	Later operation	Local symptom free	Local recurrence
Stage Ia	13	6	2	5	13	0
Stage Ib	21	15	2	4	20*	1
Stage I	34	21	4	9	33*	1
Stage II	24	10	1	13	20*	4
Stage III	6	6			1†	5
	64	37	5	22	54	10

* Of whom 1 dead from intercurrent disease.
† Dead, progressive glandular metastases.

Of the total material of 72 patients, no less than 64 have received primary radiation treatment, 37 this treatment only. Of the 37 cases, 28 are alive and symptom free. Two have died free of symptoms and from intercurrent disease three and two years respectively after the treatment, whereas 7 have died from or with local recurrence.

In 27 of the 64 primary irradiated cases has remaining tumor or recurrence later made surgical intervention necessary (electrocoagulation in 5 and amputation of the penis in 22 cases). Of these, 24 are locally symptom free, 3 have died with local recurrence.

For illustration of radiosensitivity of cancer of the penis the material supplies the information that complete destruction of the primary tumor after irradiation has been obtained in 30 of 64 cases in all stages; that is, in nearly half the number of cases (46.9 per cent). Considering only Stages I and II—the really tractable ones—it is seen that of 64 patients 58 received primary irradiation, which in 31 was the only treatment. In the latter cases a satisfactory local effect has been obtained in 29: that is, in exactly half the number of all primary irradiated cases.

Also in most of the patients in whom operation has later become necessary, there has been a marked radiation effect, in some primary clinical freedom from symptoms. Further, we have the definite impression that irradiation has offered the advantage of permitting a more conservative surgical intervention, where this has later had to be done. We also feel justified in concluding from the material that in cases where operation has become necessary in spite of preceding radiation treatment the postponement of the operation, conditioned by the primary irradiation, has by no means reduced the patients' chances for recovery. On the contrary, it seems to have had certain unquestionable advantages.

The radiation treatment has nearly always been carried out according to plan. Never has an already present infection meant an essential obstacle. In exceptional

cases only has this caused an interruption of the treatment, but never for long. No serious, prolonged radionecrosis has occurred in these cases, except in 2 cases with practically complete destruction of the penis, where some necrosis developed in an ulcerated tumor over the os pubis, around the root of the penis. However, the extent to which this necrosis was attributable to the irradiation is difficult to decide. In some other cases the healing process may have been somewhat slow, however without causing much inconvenience. In the majority of cases the course of the irradiation reaction has been practically the same as that usually seen in other regions.

We have asked ourselves the reason why our experiences with primary radiation treatment of cancer of the penis apparently are considerably better than those from many other tumor clinics, with regard to the radiosensitivity as well as to practicability of the treatment. I believe that probably the following conditions have played an essential part in this connection:

The radiation is always given using a greatly protracted or protracted-fractionated technique, either with radium on a mold or by means of teleradium. Direct contact or interstitial application (needles) is not used. In the presence of phimosis the prepuce, if at all possible, is always extirpated before irradiation, or where adhesions or tumor infiltration prevents this, partial removal is done or a slit is made, so that good drainage is provided for, and conditions obtained for the most effective control during the further course.

SUMMARY

A material consisting of 72 cases of cancer of the penis treated at the Norwegian Radium Hospital is here reported. Sixty-four of these cases have had primary radiation treatment, in 37 of which it was the only treatment (apart from phimosis operation). Of the latter 28 are locally symptom free, 2 have died symptom free from intercurrent disease, and 7 have died with local recurrence. Because of remaining tumor or recurrence surgical intervention (electrocoagulation in 5 and amputation of the penis in 22 cases) has later become necessary in 27 cases. Of these 24 are locally symptom free, while 3 have died with local recurrence. In the total material freedom from symptoms after three and five years respectively has been found in: 93.3 per cent of 15 and in 100 per cent of 11 cases respectively in Stage Ia, in 85.7 per cent of 21 and in 81.3 per cent of 16 respectively in Stage Ib. Stage I in all: 88.9 per cent of 36 and 88.9 per cent of 27 respectively. Stage II: 67.9 per cent of 28 and 63.6 per cent of 22 cases respectively. Stage III: 0. Total material: 70.8 per cent of 72 and 66.7 per cent of 57 patients respectively.

The following method of treatment has been used: phimosis operation followed by radium treatment (on a mold or with teleradium) that is given greatly protracted or protracted-fractionated. For persistent or recurrent tumor a comparatively conservative amputation of the penis is done or, in a few cases, electrocoagulation is used. The lymphatic regions are always irradiated (*as a rule with teleradium*) whether or not metastases are clinically demonstrated. For persistent, newly formed or recurrent glandular metastases dissection of the groins is done.

This method allows the treatment to be carried out without complications, and the radiosensitivity is rather good. The percentage of cases in which freedom from symptoms has been obtained compares with or surpasses the results observed after more radical treatment methods. Also the functional results are better.

Norwegian Radium Hospital
Oslo, Norway

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CARCINOMA OF THE ANAL CANAL*

STATISTICS OF THE FONDATION CURIE, PARIS

By J. L. ROUX-BERGER *and* A. ENNUYER

Fondation Curie

PARIS, FRANCE

INTRODUCTION

ON READING the literature concerning carcinoma of the anal canal, one is struck by the fact that, as a rule, no clear distinction is made between this and carcinoma of the rectum. The two are usually classified together as one lesion in most of the published works. It is difficult to justify this association, but it may partly be explained by the fact that the lower end of the rectum is almost constantly invaded by carcinoma arising in the anal canal, if it is at all extensive.

Without going into the exact anatomical details, which we consider unnecessary here, we wish to state at the very beginning that the anal canal proper is limited to a very small portion of the digestive tract, averaging about 2 centimeters in length. Carcinoma arising in its wall can therefore remain localized to it only for a very short time. Judging from the extent of most of the tumors in this site which we have treated, it appears certain that the lowest portion of the rectum must have been involved in almost every case.

Despite this, it is important to distinguish between those cases of carcinoma arising primarily in the anal canal and these arising in the rectum, because of the following important properties of anal lesions:

(1) Greater accessibility of the tumor for irradiation.

(2) Its proximity to the anal sphincter which cannot be preserved by surgical treatment of the lesion.

(3) Its histopathological structure. All the lesions of our series were of epithelial origin and therefore considerably more radiosensitive than adenocarcinoma of the rectum.

(4) Rarity with which it results in intrapelvic lymph node metastases which are common in carcinoma of the rectum. These lesions tend more to involve the inguinal lymph nodes.

The study of anal carcinoma as a separate entity is made more difficult still by the rarity of its occurrence. For instance, at the Anti-Cancer Centre of Liège (Belgium) for 4,000 patients its percentage incidence was only 0.45 per cent. Here at the Fondation Curie out of 10,000 patients, only 0.58 per cent had true anal lesions. Furthermore the few statistical analyses which have been published concerning this lesion suffer from the disadvantage that they concern only a small number of cases and even these are not followed up for a sufficiently long period of time (generally one to three years). As far as we could determine, no important five year results have been published. This makes comparison of the various methods of treatment, either radiotherapeutic or surgical, difficult.

This may explain the evident divergence of opinion which exists. For instance Bensaude states, "Radium can cure anal carcinoma in the great majority of cases," whereas Duckerts considers that carcinoma arising in this site carries a much graver prognosis. "In our series" he says, "only 1 case in 26, i.e. 3.8 per cent has responded favorably to treatment" (a five year cure).

We intend to deal with the subject under three principal headings:

I. Results of treatment of carcinoma of the anal canal, 1921–1940.

II. Results of treatment of carcinoma of the anal margin, 1921–1940.

III. Account of some modifications in treatment methods introduced since 1940,

* From the Departments of Clinics and Therapeutics of the Fondation Curie, Director J. L. Roux-Berger.

but which have not been sufficiently long in use to yield proper statistical results.

I. RESULTS OF TREATMENT OF CARCINOMA OF THE ANAL CANAL, 1921–1940

This first part concerns 51 cases of carcinoma of the anal canal treated between 1921 to 1940. Throughout the paper the word cure denotes a patient alive and well five years or more after the treatment.

Among these 51 cases we have obtained 18 cures; 13 of these exceeded the five year limit; varying from a period just over five years to sixteen years and averaging nine years.

The functional results in the 18 five year cures were as follows:

3 cases of complete anal stenosis with 3 colostomies.
3 cases of partial anal stenosis with 3 colostomies.
1 case of slight anal stenosis with 1 colostomy.
11 cases of normal ani all without colostomy.

Analysis of the 33 failures is as follows:

21 cases of failure to sterilize the tumor.
2 cases of recurrence in the lymph node areas; one of these in the pelvic nodes and the other in the inguinal nodes.
3 cases of recurrence of both primary and lymph areas.
1 case of metastasis in the lumbar vertebrae.
4 deaths due to intercurrent disease.
2 patients untraced.

Analysis of these results according to the extent of the lesion: In dealing with this aspect we must take into account both the extent of the primary tumors and that of any lymph node metastasis present.

It is not difficult to determine the circular extent of the primary lesion around the anal canal, but it is more difficult to be precise about its extent upwards into the rectum. But as we have stated before, this involvement of the rectum must occur in most cases, owing to the shortness of the anal canal. For purposes of precise analysis, we have divided tumors invading the rectum into two classes.

(a) Tumors invading the rectum slightly (i.e. less than 5 cm. in length).

(b) Tumors invading the rectum extensively (i.e. more than 5 cm. in length).

The existence of lymph node metastasis can only be determined with certainty by the histopathological examination of specimens removed from patients who have undergone block dissection of the groins, or in those cases in which prolonged and careful clinical observation leaves no doubt as to their presence or absence. However, not many of our patients have had inguinal block dissection performed. In other cases, rapid advance of the primary lesion has caused the death of the patient before a sufficient length of time had elapsed for proper observation of the lymph node areas. These facts have made accurate statistics impossible to obtain. A similar difficulty has arisen in all sites where a routine block dissection has not been performed.

Analysis of results according to extent of primary lesion:

(1) Small lesions of the anal canal which do not completely surround it, but extend more or less widely byond the anal margin on to the perianal skin.

3 cases—2 cures and 1 failure.

The lesion cured in both the cases was a small one.

In the third case the lesion extended far beyond the anal margin onto the perianal skin. The patient died of perianal gangrene, immediately following radium implantation.

(2) Lesions completely limited to the anal canal (i.e., less than 2 cm. in length). In our series none of these cases had lesions completely surrounding the canal; one wall was always found uninvaded at rectal examination.

(3) Lesions involving the rectum slightly (less than 5 cm. in length).

16 cases—6 cures—10 failures.

(4) Lesions invading the rectum extensively (more than 5 cm. in length).

18 cases—4 cures—14 failures.

(5) Lesions with lateral extension into the ischiorectal fossa:

4 cases—no cures—4 failures.

Analysis of lymph node metastasis:

1. Cures with enlarged inguinal nodes.

Twenty-eight of our 51 cases had clinically enlarged inguinal lymph nodes. Treatment was as follows:

(a) Surgical treatment: 8 cases

Histopathological examination of the removed specimens revealed:

6 cases with proved metastases (nodes markedly enlarged).

2 cases without metastases (enlargement of the nodes here not marked).

Of the 6 cases with proved metastases:

Two subsequently developed recurrences; 1 of these after five years (primary lesion not sterilized) and the other after two years (primary lesion healed). One died two years afterwards exact cause unknown. One died one year afterwards of jaundice; no evidence of recurrence present.

One patient alive six years later; no information as to local condition.

One of the 2 cases in which the histopathological examination was negative was alive seven years later.

One was alive and well four years later and the other untreated after fifteen months

(b) Treatment by radiotherapy:

7 cases treated; no subsequent evidence of recurrence.

(c) Cases with enlarged lymph nodes observed but not treated.

13 cases, 1 recurrence in the tenth year (primary lesion healed). The others showed no evidence of recurrence.

2. Cases with enlarged pelvic lymph nodes (revealed by rectal examination).

Invasion of the pelvic lymph nodes was found in 5 cases out of 51. In all of these cases the rectum had been invaded by carcinoma. Only 1 of these showed subsequent evidence of carcinoma.

The conclusions we draw from this analysis of the extent of the lesions are as follows.

(1) Concerning the primary lesions: Size is of great prognostic importance. Although the small number of cases in our series does not give us the right to establish percentages, it is sufficiently clear from what is written regarding the extent of the primary lesions that the curability of the tumor depends largely on its extent and therefore on early treatment.

This early treatment has been achieved by certain American authors who practice routine microscopic examination of all anal lesions. Thus Buie has discovered 18 cases of carcinoma not clinically recognized as such (in 951 histopathological examinations).

(2) Concerning the lymph nodes: Conclusions are not so easily drawn. It is obvivious that our estimation of the indications of surgery is satisfactory since out of 8 cases operated upon, 6 had microscopically proved metastasis. But it is not possible to draw any conclusion concerning the cases which have undergone radiotherapy. These cases have shown no sign of subsequent recurrence, it is true, but among these cases with clinically enlarged lymph nodes with no active treatment, only 1 developed subsequent lymph node metastasis after ten years.

On the strength of these figures, it seems probable that no treatment of the lymph node areas is required, when the clinical examination does not reveal enlarged nodes or even in the cases where the enlargement is not marked and does not present definite signs of malignancy.

There is another fact which supports this conclusion, namely, that these cases have been followed for long periods of time. For the 36 cases where lymph nodes areas received no treatment, the period of observation ranges from six months to sixteen years and in 10 of these was of more than five years. In all these, only 2 subsequently showed evidence of metastasis.

Taking into account this rarity of lymphatic recurrence, we are then forced to conclude that block dissection of lymph drainage areas is not so imperative as in carcinoma arising in other sites provided the patients are kept under careful observation.

More decisive conclusions than this will be determined only by statistics of a larger number of cases, followed for a longer period of time, e.g. for ten years.

Histopathology and Radiosensitivity.

The results of histopathological examination of the biopsies are as follows:

Differentiated squamous carcinoma—38 cases
Anaplastic carcinoma—13 cases

Two of the anaplastic carcinomas showed areas of cylindromatous development.

The distinction between squamous carcinoma and anaplastic carcinoma is not always definite. The site and the extent of the biopsy taken may affect the pathological report as characteristics of the lesion may change from area to area throughout its extent. Moreover, in one case in which the primary tumor had been classed as anaplastic, the lymph node metastases were found to be squamous in type. We wish to stress the point made by Dr. Gricouroff, who has performed all the histopathological examinations, that the undifferentiated tumors of the anal canal have no connection with basal cell carcinoma of the skin which never give rise to metastatic deposits.

The following figures show the proportion of cases in which complete initial regression was obtained with radiotherapy:

Differentiated squamous carcinoma—18 cases out of 38
Anaplastic carcinoma—10 cases out of 11
(Two untraced cases are excluded)

But when we consider the five year results of treatment according to the extent of the lesions, the proportion of cures in both is almost the same.

So far as we have determined, the percentage of lymph node metastasis in both types is similar. But it must be recalled that our knowledge of the involvement of lymph nodes is very imprecise.

Surgical Treatment.

This question must be considered from several points of view: (1) Comparison of long term surgical and radiotherapeutic results: If anyone could bring forward conclusive statistics in favor of either surgery or radiotherapy, the question of the best treatment would no longer be open to dispute. But such a comparison at present is impossible, as there are no statistics of importance concerning five year results in either field. In all the literature which we have had access to, we have found reports of only 10 five year cures by surgery and 10 by radiotherapy. Even these cannot be translated into percentage figures because nearly all these reports include cases which have not been followed up for five years (see Tables I and II).

TABLE I

SURGICAL CURES OF AT LEAST FIVE YEARS' DURATION

Raiford	(1933)	1 case
Pemberton and Dixon (Mayo Clinic)	(1934)	3 cases
Keyes	(1937)	4 cases
Cattell	(1943)	2 cases
		10 cases

TABLE II

CURES BY RADIOTHERAPY OF AT LEAST FIVE YEARS' DURATION

Gordon-Watson	(1932)	1 case
Binkley	(1938)	1 case
Tucker and Hellwig	(1938)	1 case
Berven	(1939)	4 cases
Kaplan and Rubenfeld	(1940)	1 case
Meland	(1940)	3 cases
		11 cases

(2) Comparison of postoperative and postirradiation complications: Following

perineal amputation of the anal canal rapid healing occurs in most cases and after the first few days the patient has little or no pain. Following radiotherapy the radiation reaction is more unpleasant than this and varies greatly with the dose administered and the sensitivity of the patient to radiation.

(3) The question of colostomy: In choosing between various methods of treatment, is is important to take into consideration how much it means to the patient if a permanent colostomy can be avoided.

Perineal amputation of the anal canal systematically removes the sphincter and leaves the patient either with anal incontinence, or with a colostomy. It is unnecessary to enlarge on the distressing nature of this disability, even when the best care can be obtained for it. Even if the long term results were found to be exactly the same with each method, radiotherapy would have the great advantage that it gives a a chance of cure without a permanent colostomy. Among our 18 five year cures, 11 did not require this operation, and were able to defecate normally afterwards. According to these results given a lesion which is not very advanced, one may hope to preserve normal anal function for the patient by means of radiotherapy.

(4) Enlarged lymph nodes: We have already discussed lymphatic metastasis at this site. It seems that routine treatment of the lymph drainage areas is not as important as in certain cancers at other sites, e.g., the tongue. But we do think, however, that it is necessary to treat the groins whenever the clinical examination reveals enlarged nodes of apparent significance and that complete block dissection is the most effective method of doing this.

(5) Perineal amputation after the failure of radiotherapy: We have employed this procedure in 5 cases at periods varying from one to eleven months following radiation treatment. A perineal amputation of the rectum was performed followed by bilateral block dissection of the inguinal nodes. In one case the posterior vaginal wall was also removed, and in another the uterus and vagina.

Among these 5 patients:

One died of obstructive jaundice one year after operation.

A second died of local recurrence two years after operation.

A third died of lymph node metastasis five years after operation.

A fourth was alive and well five years after operation.

A fifth was alive five years after operation, but the condition of the treated areas was not ascertained.

We have not been able to operate on all the cases in which radiotherapy had apparently failed to effect a cure. Sometimes the extent of the lesions has been too great and we were deterred by the danger of postoperative necrosis.

Lately we have operated on such cases without complications other than delayed healing of the wound. We are proposing, in the future, to give our indications for surgery a wider scope and to operate on all possible cases as soon as it becomes apparent that the lesion has not responded to radiotherapy. Unfortunately, it is difficult to determine exactly when hope of success by radiotherapy must be given up. Several factors must be considered before deciding on operation: histopathologic structure, size of the tumor, and the radiotherapeutic method. Tentatively we have decided that it is advisable to wait at least two months after radiotherapy in any case and then only to decide on surgical intervention if a positive biopsy report is obtained.

Radiotherapeutic Methods. The radiotherapy of these tumors is the least definite of all our treatments. Indeed, it would appear that we are undecided as to the best method to adopt, considering that for our 51 patients treated, 17 different methods of treatment have been tried using one or more of the following radiation devices: radium implantation, surface radium applicator, intracavitary radium teleradium therapy and roentgen therapy. Here is an analysis of the methods used which have yielded five year cures:

Radium implantation alone—2 cases treated, 2 cures.
Radium implantation and surface radium applicator—5 cases treated, 3 cures.
Radium implantation and intracavitary radium —1 case treated, 1 cure.
Radium implantation and teleradium treatment—11 cases treated, 7 cures.

It is not, however, possible to judge the value of the various methods from the above, as the tumors treated were not comparable. For instance, even though radium implantation has been used alone, and with success, in 2 cases, one must attribute this largely to the fact that those 2 patients had small lesions, and it is therefore not reasonable to conclude that radium implantation is the best method.

We have altered our methods between 1922 and 1940. Teleradium therapy has gradually supplanted local radium. Radium implantation has not been recently employed to give such large doses as in its early days. These changes were determined by the necessity to avoid delivering a dose of radiation to the anal sphincter which would cause sclerosis of the musculature and also to increase the dose in the deeper tissues without overdosing the superficial structures. Overdosage of the superficial tissues seems to have been one of the principal factors in producing the necroses which have occurred in our series.

Complications following radiotherapy.

(a) Radionecrosis: Among the 51 patients treated, 8 subsequently suffered from radionecrosis as follows:

One patient suffered a severe necrosis which persisted for thirteen years. This patient who was treated in 1922 received an excessive dose of radiation.

Three patients suffered slight necrosis which eventually healed and remained cured at the end of five years.

Four patients suffered radionecrosis plus recurrence.

Radionecrosis was much more common at the beginning of our series, but has become gradually rare. Six of the necroses occurred among the patients treated 1921–1931, whereas only 2 cases occurred among the patients treated 1932–1940. Evidence that the cause of necrosis in these cases was overdosage is furnished by the fact that no necrosis has been observed when the radium dose delivered was under 18 millicuries-destroyed. Stricture was a common sequel to necrosis. In one case only necrosis was not followed by stricture; but in that case, the necrosis was a small one.

(b) Strictures: Among the 18 five year cures, stenosis or stricture occurred in 7 cases. Four of these were of gradual onset due to progressive fibrosis of the perianal tissues and 3 followed necrosis.

(c) Complications of infection: We have had one very severe case of infection in a patient, aged seventy-one, suffering from an advanced carcinoma widely involving the perianal skin. Teleradium treatment had been carried out without incident, but during radium implantation the patient developed an infectious gangrene of the perianal tissues, which proved fatal in a few days.

Prognosis and analysis of cause of failure. Thirty-five per cent of all our cases treated have resulted in five year cures. The extent of the primary tumor has greatly influenced the prognosis in these cases.

The proportion of cures was three times as great in those cases where the primary tumor did not completely surround the anal canal, and was limited to its walls as in those where the rectum was perceptibly involved.

No success was obtained when the primary tumor completely encircled the anal canal, nor in those lesions which involved the ischiorectal fossa.

Extension to the inguinal glands does not seem to be of primary importance in prognosis. Among all the cases, whether treated or not, we have noted only 3 cases where death was caused by the lymph node metastasis alone.

It does not seem either, that the histopathological picture gives any indication

of the remote prognosis. At first sight there have been three times as many cures among the anaplastic carcinomas as among the differentiated types, but when the size of the primary lesion is taken into account, there does not seem to be much difference between the two types.

In certain of the cases where the treatment failed to cure the patient, the causes of failure were clear:

In 6 cases treatment was not completed owing to complications, e.g., gangrene, embolus, etc.
In 3 cases the patient died of lymph node metastasis.
In 1 case failure was due to a metastasis in the lumbar vertebrae.
In 1 case failure was due to intercurrent disease.

From this it would appear that there were fewer *local* failures of cure than the five year figures show.

Several failures followed underdosage or badly arranged dosage distribution within the tumor. For instance, one lesion 4 cm. in height was treated by radium implantation followed by a surface radium applicator of R. S. D., 1 cm., i.e. the type usually used for superficial cutaneous lesions.

II. CARCINOMA OF THE ANAL MARGIN, 1921–1940

In our series, there have only been 6 cases of carcinoma strictly limited to the anal margin, between 1921–1940.

Five were cases of squamous carcinoma, and one a basal cell carcinoma.

We have treated these patients as follows:

2 cases by radium implantation.
1 case by radium implantation, and a radium surface applicator.
1 case by radium implantation, radium surface applicator followed by excision.
1 case by interstitial radium and intracavitary radium.
1 case by interstitial radium and teleradium.

Of these cases 3 had inguinal block dissection performed and in every case the lymph nodes were found to be invaded by the carcinoma.

The results in these 6 cases were as follows:

3 patients alive and well at the end of five years.
1 death from intercurrent disease after one year.
1 death due to local and lymph node recurrence.
1 patient alive thirteen years after treatment without evidence of recurrence, but suffering from painful unhealed perineal necrosis.

Like Cattell, we think the only point worth noting about carcinoma at this site is the frequency with which the lymph nodes are invaded. But the small number of cases in the series prevents definite conclusions being drawn.

III. CHANGES IN TREATMENT METHODS SINCE 1940

Since 1940, we have been able to apply new principles to the treatment of carcinoma of the anal canal, owing to the possibility of employing supervoltage therapy and low voltage therapy.

(a) *Supervoltage Therapy*. Since 1940 in the treatment of this disease, surface radium applicator and radium implantation have been replaced by deep roentgen therapy on our new 500 kv. apparatus which was installed about this time.

We were influenced in this by the following considerations:

(1) The use of roentgen rays, generated at a higher tension than before, enabled us to deliver to the deeper parts of the tumor a better depth dose. Using an anterior field and a posterior sacrococcygeal field, the dose at a point 5 cm. from the anal orifice, within the rectum, was found to be increased from 33 per cent at 200 kv. to 48 per cent at 500 kv.

(2) The dose distribution within the tumor was found to be more homogeneous than that obtained by radium implantation or surface applicator. We hope that this will give us a higher cure rate and avoid necrosis of the superficial tissues due to overdosage.

(3) The possibility of reducing the occurrence of stricture by abandoning interstitial radium, which when implanted in the sphincter or its neighborhood, caused what we might call "sleeves of fibrosis" around the site of each container.

We cannot, at present, give any details of the results obtained by this method, because the follow up time for these cases is under five years. Eleven patients have been treated in this manner by Dr. Courtial.

(b) *Short Distance Low Voltage Therapy, i.e. "Contact Roentgen Therapy."* This type of treatment has been used by Chaoul for over ten years. His success with this method in carcinoma of the rectum is well known. But Chaoul does not refer either in his articles or in his recent book, "Nahbestrahlung," to the use of this method for carcinoma of the anal canal.

With the Philips apparatus of this type which we have in use at present, the only lesions which appear to be amenable to this technique are those of small size confined to the anal canal. Infiltrating or extensive lesions require multiple fields, and this technique carries the risk of overdosage due to intersection of fields, followed by necrosis or of underdosage resulting in failure to sterilize the tumor.

The technique for irradiation of the anal canal appears to be more complex than that for the rectum. It is easy to introduce the Philips tube into the ampulla of the rectum, following caudal anesthesia, or even without any preparation. But to irradiate the mucous membrane of the anal canal properly, it is preferable to dilate the canal under intravenous anesthesia, and to introduce the tube while the anus is dilated. The use of a tube in which the rays are emitted through a lateral window, or of a tube with a conical anode emitting roentgen rays over all its surface, would simplify the technique greatly, and avoid the anesthesia and dilatation.

CONCLUSIONS

(1) Carcinoma of anal canal is a radiosensitive tumor. This is shown by the eighteen five year cures in our series of fifty-one cases (35 per cent).

(2) Radiation is the only treatment which gives a chance of avoiding permanent colostomy.

(3) Comparison of radiotherapeutic and surgical results is impossible for want of extensive five year statistics.

(4) The number of failures following radiotherapy is still large. But if the treatment were carried out earlier when the lesions were still small, the number of cures would greatly be increased. *For the eleven cases where the primary lesion did not extend beyond the limits of the anal canal at treatment seven were cured.* It is curious that such painful lesions causing functional disorders at an early stage should not come to treatment until they are advanced. This is not always the fault of the patient. Routine microscopic examination seems to be of importance in an early diagnosis, since it has enabled Buie, for instance, to detect several cases of early carcinoma which had not been clinically diagnosed. It is also reasonable to suppose that the recent improvements in technique ought to give rise to better results.

The future will show whether we have been correct in abandoning radium implantation in favor of contact roentgen therapy for small lesions and supervoltage roentgen therapy for larger lesions extending outside the anal canal.

In case of failure following radiotherapy, perineal amputation of the rectum must take a greater part than hitherto. We must take into account when planning our treatment, without sacrificing any of its efficacy, that contact roentgen therapy does not affect the subsequent surgical operation, whereas operation following deep roentgen therapy carries a greater risk of necrosis on this account.

Finally, we feel that the hope of preserving a normal anus, the results that we have obtained in the past, and the technical improvements, which are at present in operation, justify the use of irradiation as the primary treatment. Subsequently, if this fails, surgical removal can be carried out, provided the previous radiotherapy has not made operation impossible.

Fondation Curie
26, Rue d'Ulm
Paris 5e, France

REFERENCES

1. Bacon, H. E. Multiple malignant tumors, with involvement of the lower bowel. *Am. J. Cancer*, 1939, *35*, 243–257.
2. Bacon, H. E., and Gilbert, P. D. Sites of metastases from carcinoma of anus, rectum and sigmoid colon. *J.A.M.A.*, 1938, *111*, 219–221.
3. Bensaude, R., Cain, A., Oury, P., and Poirier. Le cancer de l'anus. *Presse méd.*, 1933, *41*, 1837–1842.
4. Bensaude, R., Cain, A., and Hillemand, P. Le lymphosarcome ano-rectal. *Arch. d. mal. de l'app. digestif*, 1934, *24*, 875–879.
5. Berven, E. Radiological treatment of cancer of the rectum. *Acta radiol.*, 1939, *20*, 373–390.
6. Binkley, G. E. Results of radiation therapy in primary operable rectal and anal cancer. *Radiology*, 1938, *31*, 724–728.
7. Buie, L. A., and Brust, J. C. M. Malignant anal lesions of epithelial origin. *Journal-Lancet*, 1933, *53*, 565–571.
8. David, V. C., and Loring, M. Relation of chronic inflammation and especially lymphogranuloma inguinale to development of squamous cell carcinoma of rectum. *Ann. Surg.*, 1939, *109*, 837–843.
9. Dixon, C. F., and Stuart, H. A. Anorectal carcinoma. *Proc. Staff Meet., Mayo Clin.*, 1935, *10*, 798–800.
10. Dobocharevitch. Thèse de Lyon, 1923–1924.
11. Drueck, C. J. Status of physical measures in treatment of anal and rectal diseases. *Arch. Physical Therapy*, 1938, *9*, 403–407.
12. Duckerts, J. Contribution à l'étude des cancers ano-rectaux. *Rev. belge sc. méd.*, 1945, *15*, 125–156.
13. Gernez, L. L'électro-chirurgie dans certaines formes de cancers ano-rectaux. *Bull. et mém. Soc. nat. de chir.*, 1935, *61*, 1213–1219.
14. Gordon-Watson, C. Some experiences in treatment of carcinoma of rectum with radium. *Surg., Gynec. & Obst.*, 1932, *54*, 307–311.
15. Gordon-Watson, C., and Regaud, C. Discussion on radium treatment of malignant disease of rectum and anus. *Proc. Roy. Soc. Med.*, 1935, *28*, 1251–1263.
16. Hankins, F. D., and Harding, W. G., Jr. Acanthoma of anus. *Arch. Surg.*, 1934, *29*, 77–84.
17. Hartmann, H. Chirurgie du rectum. Masson et Cie, Paris, 1931.
18. Kaplan, I. I., and Rubenfeld, S. Carcinoma of the anus; its incidence, pathology and radiation treatment. Am. J. Roentgenol. & Rad. Therapy, 1940, *44*, 265–269.
19. Kerr, J. G. Squamous cell carcinoma of anorectal region. *Texas State J. Med.*, 1940, *36*, 548–551.
20. Keyes, E. L. Squamous cell carcinoma of the lower rectum and anus. *Ann. Surg.*, 1937, *106*, 1046.
21. Lacassagne, A. Résultats obtenus à l'Institut du Radium de Paris en radiothérapie des cancers du rectum. *Arch. d. mal. de l'app. digestif*, 1931, *21*, 465–471.
22. Lockhart-Mummery, J. P. *Proc. Roy. Soc. Med.*, 1933, *26*, 589.
23. Meland, O. N. Carcinoma of anus. Am. J. Roentgenol. & Rad. Therapy, 1940, *43*, 706–710.
24. Meland, O. N. What can one expect from radiation in carcinoma of rectum and anus? *California & West. Med.*, 1939, *50*, 403–407.
25. Niedermayr, R. Die kombinierte Radium-Röntgenbehandlung der Rektum- und Analkarzinome. *Strahlentherapie*, 1937, *58*, 624–631.
26. Pack, G. T. Pathological aspects of anal and rectal neoplasia. *Internat. Clin.*, 1927, *2*, 77–90.
27. Pemberton, J. deJ., and Dixon, C. F. Summary of end-results of treatment of malignancy of thyroid gland and colon, including rectum and anus. *Surg., Gynec. & Obst.*, 1934, *58*, 462–464.
28. Petrov, N. N. Therapeutic procedure in various localizations of rectal cancer. *Vestnik khir.*, 1939, *57*, 125–132.
29. Plisson, L. Epithélioma ano-rectal. *Progrès méd.*, 1927, *42*, 1408–1420.
30. Raiford, T. S. Epitheliomata of the lower rectum and anus. *Surg., Gynec. & Obst.*, 1933, *57*, 21–35.
31. Regaud, C. Traitement du rectum et de l'anus à l'Institut du Radium de l'Université de Paris. *Radiophys. et radiothérapie*, 1937, *3*, 429–436.
32. Rosser, C. Etiology of anal cancer. *Am. J. Surg.*, 1931, *11*, 328–333.
33. Rouvière, H. Anatomie des lymphatiques de l'homme. Masson et Cie, Paris, 1932.
34. Schreiner, B. F., and O'Brien, J. P. Study of 210 cases of carcinoma of rectum and anal canal, treated between 1914 and 1925 inclusive. Am. J. Roentgenol. & Rad. Therapy, 1931, *25*, 654–658.
35. Smith, N. D., and Broders, A. C. Melano-epithelioma and haemangio-endothelioma. *Surg., Gynec. & Obst.*, 1935, *60*, 74–77.
36. Tailhefer, A. Traitement des cancers du rectum et de l'anus. *Paris méd.*, 1933, *1*, 254–260.
37. Tailhefer, A., and Courtial. *Bull. du cancer*, 1943, *31*, 85.
38. Tucker, C. C., and Hellwig, C. A. Proctologic tumors. *J.A.M.A.*, 1938, *111*, 1270–1273.
39. Willan, R. J. Case of sarcoma of anus. *Brit. J. Surg.*, 1928, *16*, 161–162.

APPLICATIONS OF ARTIFICIALLY RADIOACTIVE ISOTOPES IN THERAPY*

I. COBALT^{60}

By WILLIAM G. MYERS, PH.D., M.D.
Julius F. Stone Fellow in Medical (Bio-Physical) Research, College of Medicine, The Ohio State University
COLUMBUS, OHIO

THE announcement[1] of the availability in large quantities of artificially radioactive isotopes of many of the elements, either generated by exposure to the high neutron fluxes in a nuclear reactor (pile) or resulting as by-products of controlled nuclear fission in the production of plutonium, ushered in a new era in medical science. New tools have been provided in abundance to challenge the ingenuity of the investigator in the application of them both in research and in therapy. A perusal of the lists in the publication revealed that several of the radioisotopes have properties which invite investigation of them as sources of ionizing radiation that, for one reason or another, might be used advantageously in therapy to supplement or to supplant radium and radon.

In order to augment the broad program in progress at the Ohio State University College of Medicine during the past eight years in which artificial radioisotopes have played an increasingly important role both in therapy and in fundamental research, it was decided to survey systematically several of the radioactive isotopes now at hand in adequate amounts and activities for the first time, to discover those which will prove to be the most useful directly in therapy. Cobalt^{60} was chosen for the initial investigation principally because its relatively long half-life of more than five years would facilitate the accumulation of experience with the new sources of ionizing radiation. It was originally planned to review the pertinent physical properties of the radioisotope and to present the advantages of the form in which we had found it to be suitable after a time when we had had the opportunity to gain at least preliminary clinical experience with it to report simultaneously.† But the wide interest created recently by the disclosure to the Press by the Chairman of the United States Atomic Energy Commission that research was in progress at several universities, including The Ohio State University, on possible therapeutic applications of radiocobalt, makes it appear desirable at this time to summarize the physical properties together with our experience with the isotope thus far.

PHYSICAL PROPERTIES OF COBALT^{60}

Cobalt^{60} can be generated conveniently by the reactions:

$$(1)\qquad {}_{27}Co^{59} \xrightarrow[\text{(Nuclear Reactor)}]{n,\ \gamma} {}_{27}Co^{60}$$

$$(2)\qquad {}_{27}Co^{59} \xrightarrow[\text{(Cyclotron)}]{d,\ p} {}_{27}Co^{60}$$

In the first reaction, a neutron is captured by the nucleus of the stable isotope of cobalt of mass 59,[2,3,4,5,7,9] which comprises all of the natural element[6] to convert it to Co^{60} with the simultaneous emission of a gamma photon in the process.[2] Since a nuclear reactor is an excellent source of controlled high neutron fluxes, this nuclear reaction goes very efficiently when cobalt is placed within it. In the second reaction, the neutron from a deuteron bombarding

† Professor Joseph L. Morton, who has recently resumed his duties in the Radiology Department of The Ohio State University after a leave of absence, will direct the studies at this institution leading to the clinical evaluation of the usefulness of Co^{60} in therapy. His encouragement largely led to the initiation of these early studies.

* Presented at the Thirtieth Annual Meeting, American Radium Society, Chicago, Ill., June 20–22, 1948.

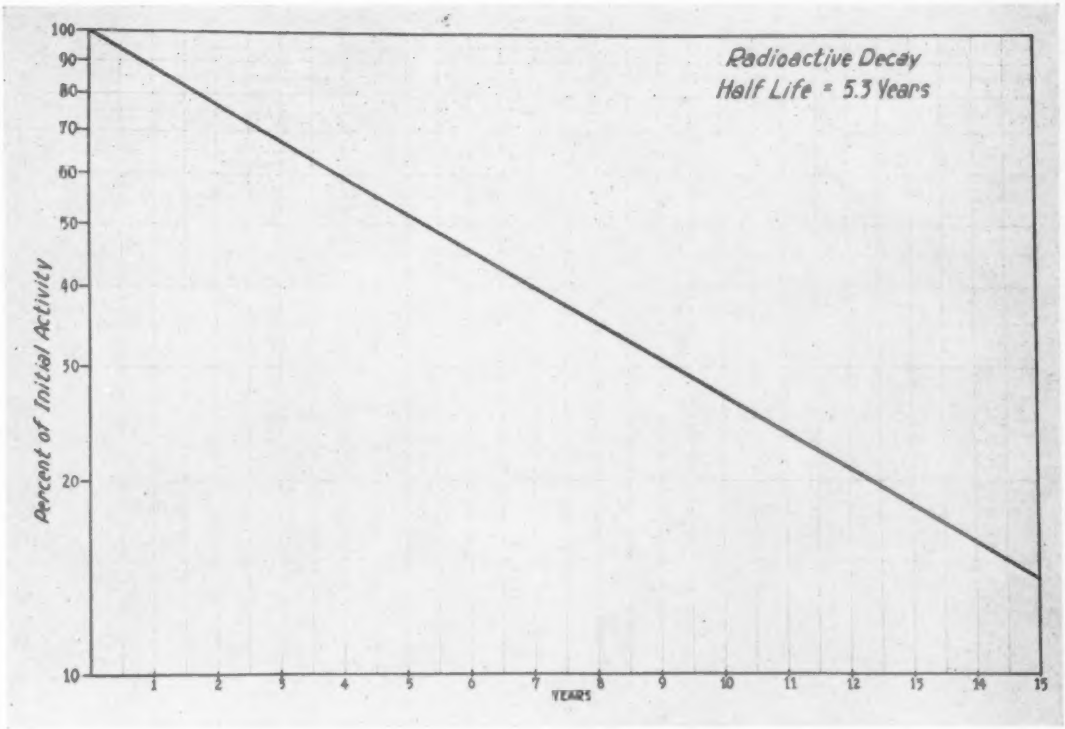

FIG. 1. Decay curve for a radioisotope with half-life of 5.3 years.

Co^{59} in a cyclotron is captured by the nucleus and the proton is rejected.[7,8,9] In both instances isomeric radioactive nuclei with half-lives of 10.7 minutes and 5.3 years may be formed.[7,8] Obviously the short-lived isomer is of no importance in therapy. Only a small part of Co^{60} generated in a nuclear reactor is the 10.7 minute isomer and probably most of that which does form disintegrates by isomeric transition to the long-lived isotope.[7,8,9] In Figure 1 there appears the radioactive decay curve for an isotope with a half-life of 5.3 years* and in Table 1 are listed the calculated percentages of the initial activities remaining at monthly intervals together with the reciprocals. Figure 2 depicts the disintegration scheme of the long-lived Co^{60} isotope according to Professor Robley D. Evans.[11] It is seen from this that the emission of an

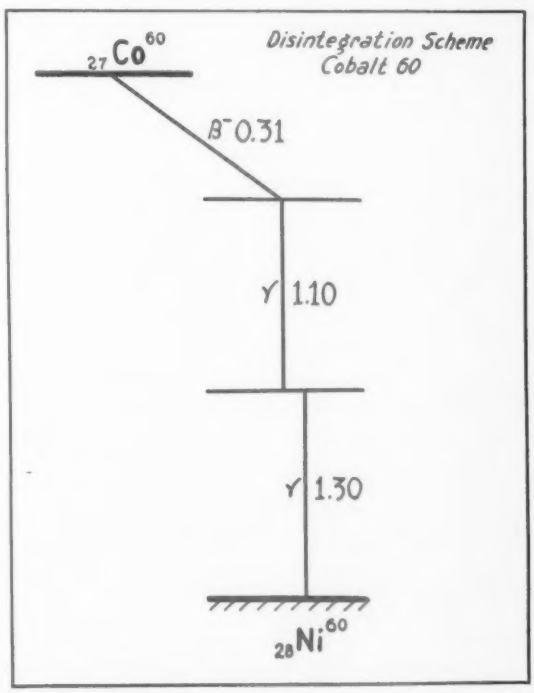

FIG. 2. Disintegration scheme of long-lived cobalt^{60} (after R. D. Evans).

* Dr. L. F. Curtiss recently stated at a meeting of the Biology Division of Argonne National Laboratory that the 5.3 year half-life value for the long period Co^{60} isotope is proving to be accurate to within 1–2 per cent on the basis of early reports from two different laboratories where it is being checked.

TABLE I

PERCENTAGES AND RECIPROCALS OF THE INITIAL ACTIVITY REMAINING AT MONTHLY INTERVALS CALCULATED FOR A RADIOISOTOPE WITH HALF-LIFE = 5.3 YEARS

Time Yr.	Mo.	Per Cent Remaining	Reciprocals	Time Yr.	Mo.	Per Cent Remaining	Reciprocals	Time Yr.	Mo.	Per Cent Remaining	Reciprocals
	0	100.00	1.000	3	9	61.23	1.633	9	0	30.82	3.244
	1	98.92	1.011		10	60.55	1.651		2	30.15	3.316
	2	97.83	1.022		11	59.91	1.669		4	29.50	3.389
	3	96.78	1.033	4	0	59.27	1.687		6	28.86	3.465
	4	95.73	1.044		1	58.61	1.706		8	28.24	3.541
	5	94.70	1.055		2	57.98	1.724		10	27.63	3.619
	6	93.67	1.067		3	57.35	1.743	10	0	27.03	3.699
	7	92.66	1.079		4	56.72	1.763		2	26.45	3.780
	8	91.64	1.091		5	56.11	1.782		4	25.88	3.863
	9	90.66	1.103		6	55.51	1.801		6	25.32	3.949
	10	89.68	1.115		7	54.90	1.821		8	24.78	4.035
	11	88.70	1.127		8	54.31	1.841		10	24.25	4.123
1	0	87.74	1.139		9	53.72	1.861	11	0	23.72	4.215
	1	86.80	1.152		10	53.14	1.881		2	23.21	4.308
	2	85.85	1.164		11	52.56	1.902		4	22.71	4.403
	3	84.91	1.177	5	0	52.00	1.923		6	22.22	4.500
	4	84.00	1.190		1	51.42	1.944		8	21.74	4.599
	5	83.06	1.203		2	50.87	1.965		10	21.28	4.699
	6	82.19	1.216		3	50.32	1.987	12	0	20.81	4.805
	7	81.30	1.230		4	49.77	2.009		6	19.50	5.128
	8	80.40	1.243		5	49.23	2.031	13	0	18.26	5.476
	9	79.53	1.257		6	48.71	2.052		6	17.10	5.847
	10	78.69	1.270		7	48.18	2.075	14	0	16.02	6.242
	11	77.81	1.285		8	47.65	2.098		6	15.01	6.662
2	0	76.99	1.298		9	47.14	2.121	15	0	14.06	7.112
	1	76.14	1.313		10	46.62	2.145		6	13.17	7.593
	2	75.31	1.327		11	46.12	2.168	16	0	12.33	8.110
	3	74.50	1.342	6	0	45.62	2.192		6	11.55	8.658
	4	73.70	1.356		2	44.64	2.240	17	0	10.82	9.242
	5	72.91	1.371		4	43.67	2.289		6	10.14	9.861
	6	72.11	1.386		6	42.74	2.339	18	0	9.49	10.537
	7	71.33	1.401		8	41.81	2.391		6	8.89	11.24
	8	70.55	1.417		10	40.91	2.444	19	0	8.33	12.00
	9	69.79	1.432	7	0	40.03	2.498		6	7.80	12.82
	10	69.05	1.448		2	39.16	2.553	20	0	7.31	13.67
	11	68.28	1.464		4	38.32	2.609		6	6.85	14.59
3	0	67.54	1.480		6	37.50	2.666	21	0	6.41	15.60
	1	66.81	1.496		8	36.68	2.726	22	0	5.64	17.73
	2	66.09	1.513		10	35.89	2.786	23	0	4.94	20.24
	3	65.37	1.529	8	0	35.12	2.847	24	0	4.33	23.09
	4	64.66	1.546		2	34.36	2.910	25	0	3.80	26.31
	5	63.96	1.563		4	33.62	2.974	30	0	1.98	50.50
	6	63.27	1.580		6	32.90	3.039	35	0	1.03	97.08
	7	62.57	1.598		8	32.19	3.106	40	0	0.535	186.8
	8	61.90	1.615		10	31.49	3.175	50	0	0.145	690.0

electron with $E_{max.} = 0.31$ mev. is followed by two gamma photons in cascade with energies of 1.10 and 1.30 mev. respectively.[9,10] In Figure 3 is shown the absorption of the gamma radiation by lead. The half-thickness is found to be 0.44 inch corresponding to a photon energy of about 1.35 mev.

APPLICATORS CONTAINING COBALT[60]

Elemental cobalt as it is usually obtained is a hard, brittle, and highly magnetic metal with a melting point of 1,480° C. and a density of 8.9. It is available commercially in the form of rondels at a few dollars a pound. These proved to be so hard and difficult to machine that an alloy was sought which would be more workable and the other component of which would not emit significant amounts of undesirable radiation after bombardment in the nuclear reactor. An inexpensive alloy composed of 45 per cent cobalt and 55 per cent nickel* known as "cobanic" is proving to be highly

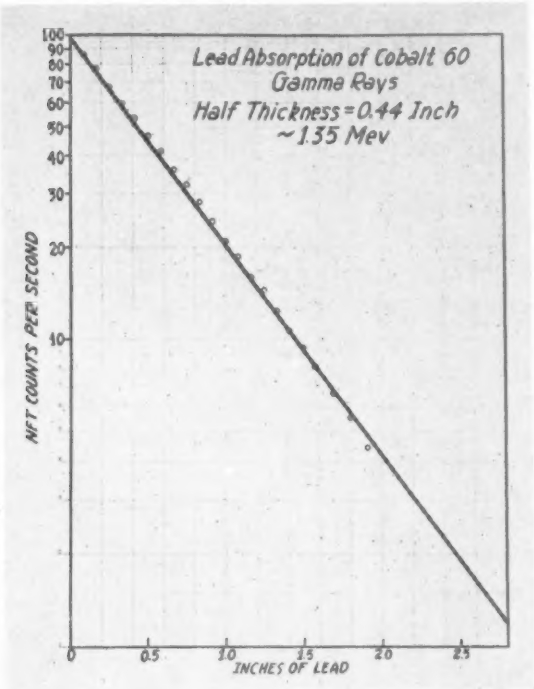

Fig. 3. Absorption of gamma radiation emitted from cobalt[60] by lead.

satisfactory for our purpose. Cobanic has been obtained† in the form of wire in several diameters. The wire is hard and stiff, though it can be machined fairly readily in the temper at hand. A wire 0.040 inch in diameter broke only after more than a dozen sharp 90° bends. It is highly inert chemically as evidenced by essentially no

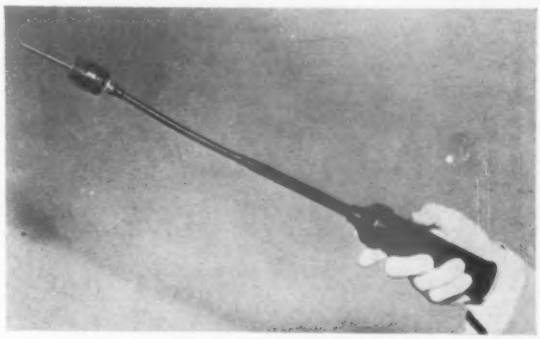

Fig. 4. Battery-operated electromagnet with semi-flexible shank for operations around shields.

observable change in the surfaces of pieces immersed in 0.1 N hydrochloric acid and 0.1 N sodium hydroxide respectively for the past year. It is strongly magnetic and we have found it most convenient to handle it during many manipulations with an electromagnet* both before and after irradiation in the pile. A very useful magnet attached in place of the bulb on the end of a long probe-type flashlight and operated by two small dry-cells is shown in Figure 4.‡ The shank is semi-flexible and can be bent to work around shields. The components of a piece of cobanic wire were separated chemically§ after activation and it was found that any radionickel generated during the bombardment does not contribute significantly to the total radioactivity emitted by the piece of wire.

We have found it convenient to cut cobanic wire 1 millimeter (18 gauge, 0.040 inch) in diameter into cylinders 1 centimeter long in the apparatus shown in Figure 5¶ which is readily adjustable both

* Suggested by Dr. Paul C. Aebersold, Chief of Isotopes Distribution, Atomic Energy Commission, Oak Ridge, Tennessee. His cooperation has been most generous and is much appreciated.

† "Cobanic" wire was kindly furnished in several sizes by The Wilbur B. Driver Company, Newark, N. J.

‡ Designed and constructed by Mr. P. E. Weiler, Department of Physics, The Ohio State University.

§ Separated by Mr. Harmon L. Finston, Department of Chemistry, The Ohio State University.

¶ Designed and constructed by Mr. Carl McWhirt, machinist in the Department of Physics, The Ohio State University.

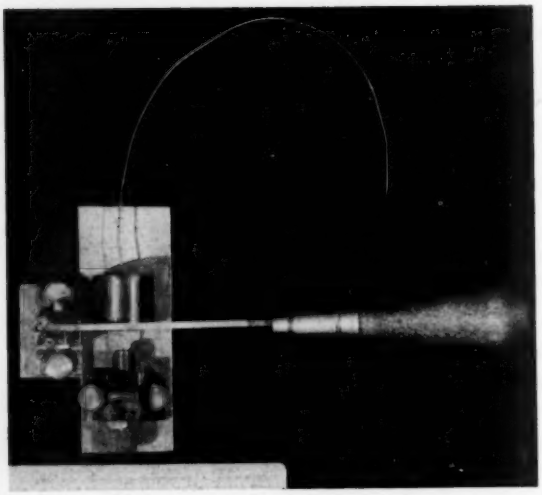

Fig. 5. Cutter adjustable for length of cut and diameter of wire.

for length of cut and diameter of wire. The cylinders made in this manner are remarkably constant in weight, 66.66 ± 0.30 milligrams each; and it is essential that this be the case for the sake of uniformity, since we find that the amount of radioactivity present in the cylinders after exposure to the neutrons in the nuclear reactor is proportional to the mass within a few per cent, when the diameters remain constant. It is a simple matter to weigh the cylinders and select those which fall within the desired limits. Each cylinder is inspected with a low-power lens and any which show burrs are either rejected or the burrs are scuffed off with fine emery cloth. In this way it is an easy task for one to prepare and select a hundred or more of the cylinders in a few hours.

After irradiation in the Oak Ridge nuclear reactor for about a month the above cylinders exhibit a gamma-ray activity approximately equivalent to that emitted by 1.0–1.5 milligrams of radium. A needle about 3 centimeters long and weighing 193 milligrams which was made from cobanic wire 1 millimeter in diameter, was found last November to emit gamma radiation equivalent to that from 4.08 milligrams of radium when the gold leaf electroscope was surrounded by 1 centimeter of lead, and showed 2.97 milliroentgens per hour at 1 meter (mrhm).* This activity is suitable for many clinical applications. If one wished it to be doubled, he would have merely to request that the time of exposure in the nuclear reactor be twice as long. Or, if the requirements were that the diameter of the wire should be less but the activity per unit length should remain unchanged approximately, the irradiation time should be increased inversely with the decreased mass of cobalt per unit of length. The converse of this principle was applied when some cylindrical slugs 1 centimeter long and weighing 1.445 grams each were cut from cobanic wire 4.6 millimeters (5 gauge, 0.185 inch) in diameter. After these were irradiated along with the 1 millimeter cylinders above in the nuclear reactor at Oak Ridge for a month, the activities were found to be 18.6 mrhm and 1.12 mrhm respectively, based on the standardized needle described above. The ratio of activities is 16.6 whereas the weight ratio is 21.7. The variation from proportionality may be accounted for on the basis of the large cross-section of cobalt for slow neutrons[12] which might be expected to result in some "shading" of the nuclei from neutrons within a relatively thick piece of the alloy by the cobalt nuclei nearer to the surface. Self-absorption of the gamma photons by the thicker pieces could also account for some of the observed lack of proportionality. Still a third way in which the amount of Co^{60} present might be varied within limits, in those cases in which it was desirable that the diameter or mass of an applicator and the time of irradiation in the nuclear reactor should remain constant, would be by increasing or decreasing the proportion of cobalt in the alloy.

Figure 6 is a photograph showing two of the large slugs and five of the small cylinders described above, together with a threaded 3 centimeter cobanic needle and one-cell and two-cell length gold alloy needle filters which are commonly employed with radium to absorb most of the high energy beta particles emitted. We

* These values were kindly determined by Dr. L. F. Curtiss at the National Bureau of Standards.

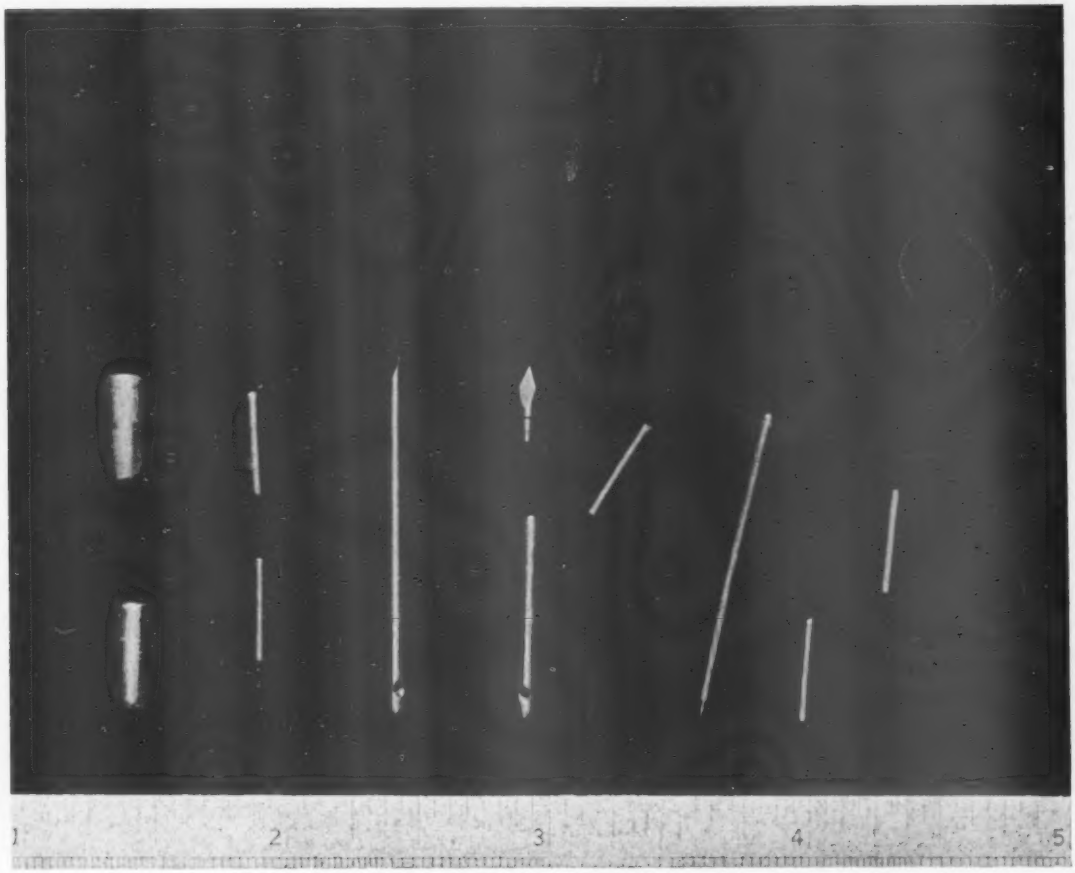

Fig. 6. Cobanic slugs, cylinders, and needle with one-cell and two-cell gold-alloy sheath needles.

have found it convenient at this stage of development to use the gold filters in our early studies to absorb the 0.31 mev. (maximum) beta particles emitted by the long-lived $Co.^{60}$ That this is necessary in order to minimize periacicular necrosis is demonstrated in Figure 7 which is a radioautograph of a radioactive cobanic needle 4 centimeters long over each end of which was slipped one of the one-cell length gold filters before placing it on the emulsion of a lantern slide for about five minutes. It is obvious that the greater density in the unshielded central portion is probably due to the beta particles which were removed by the gold alloy filters covering the ends.

The use of gold or platinum or other metals of high atomic number as filters to remove beta particles is not optimally advantageous as was clearly shown in the studies by Quimby, Marinelli and Blady,[13] and others. They found that the number of secondary electrons resulting from the gamma rays from radium traversing various filters was a minimum when the filters were made up of elements of intermediate atomic number, particularly in the range 26–50 which includes among others, iron, cobalt, nickel, copper, zinc, silver, and tin. It is anticipated that one of the foremost advantages of $cobalt^{60}$ over radium for gamma-ray therapy will prove to be the comparatively low maximum energy of the beta particles emitted, only 0.31 mev., as

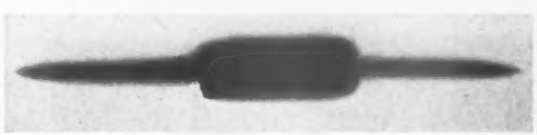

Fig. 7. Radioautograph of 4 centimeter radioactive needle containing $cobalt^{60}$ with gold-alloy sheath on each end to filter out the beta particles.

compared with maximal energies about ten times as great for beta particles given off by some of the radioactive disintegration products of radium. Because their energies are so low the beta particles can easily be removed by thin, strong, and inexpensive monel metal, stainless steel, or other filters composed of elements of intermediate atomic number. In this respect as well as the other properties it possesses as described previously, cobanic alloy itself should be very suitable material from which to make filters. It would have the advantage over many other alloys because it is strongly magnetic so that non-radioactive cobanic filters loaded with the radioactive cobanic could also be handled conveniently and safely with the electromagnet. It is necessary to use gold or platinum filters with radium, at least in large part, because the beta particles present have such high energies that they are not removed completely by thicknesses of lighter elements consistent with practicable needle diameters. In addition to the stainless steel and monel filters which we are now developing, experiments are in progress designed to electroplate about 0.1 millimeter of pure nickel on pointed and eyed cobanic needles such as the threaded needle shown in Figure 6. Calculations indicate that this thickness of nickel should be about sufficient to absorb completely all beta particles with energies of 0.31 mev. or less. The electroplating will be done before irradiation in order that the radioactive needles only 1.2 millimeters in diameter will come from the pile with filters permanently attached and ready for threading. If it were desirable, the diameter could be made even less and the activity per unit of length remain unchanged provided that the time of irradiation in the nuclear reactor were appropriately lengthened.

DISCUSSION

The essentially homogeneous gamma rays, 1.1 and 1.3 mev., emitted by Co^{60} should prove to be particularly advantageous in "telecobalt" installations. Because the isotope can be generated readily in any desired quantities and at moderate cost, the way is now open for this method of application to be come more widely applied in this country, particularly in the larger treatment centers. For large bone lesions the homogeneous high energy photons are expected to prove especially useful in comparison with the heterogeneous gamma rays emitted by radium and its disintegration products because the absorption and scattering will be more uniform.[14]

Besides the numerous advantages of cobalt^{60} over radium described above, additional ones might be listed: 1. There are no gaseous radioactive daughters and leakage is therefore impossible. 2. Because of the properties of alloys containing cobalt which are suitable for irradiation, breakage is almost completely eliminated. Moreover, if it should occur, the pieces could be recovered with no danger of loss by solution and the resultant dangers of lodgment in bones as in the case of radium. If a soluble salt of radiocobalt were present in the broken applicator for some reason, any which did dissolve would be eliminated quickly in the urine. 3. Cobalt alloys can be machined easily to any desired shape before irradiation, thus eliminating the problems and dangers associated with the uniform loading and sealing of radium in applicators. 4. If it proves feasible to prepare needles and other applicators incorporating a permanently attached electroplated nickel absorber for the soft radiocobalt beta particles, these may then be bent readily to fit lesions of different shapes.

The chief disadvantage of cobalt^{60} over radium is, obviously, the relatively short half-life of only 5.3 years compared with 1,590 years for radium. For this reason comparisons of relative costs, especially on a long-term basis, are largely meaningless. In this respect one must consider the possibility that applicators containing Co^{60} could be irradiated further, or "warmed-up" so to speak, in a nuclear reactor whenever it becomes desirable to increase the activity or to restore the waning activity due to decay.

The radiotherapist who uses cobalt^{60} will

be largely compensated for the effort he must expend in the frequent re-evaluation of his applicators, by the presence in his stock at all times after the first few acquisitions, of several different strengths from weak to strong, so that he can apply them to best advantage in formulating the Paterson-Parker patterns[15,16,17] to irradiate individual lesions most effectively. This flexibility will be especially helpful in those departments which have radiation physicists on the staff and instruments suitable for making the measurements frequently.

It hardly needs emphasis that applicators emitting photons with a half-thickness in lead of 0.44 inch must be handled with great care and with full cognizance of the possible dangers involved. In this respect the shielding problem so far as the gamma radiation is concerned is essentially the same as that encountered with radium.

It is a pleasure to express my gratitude to Professor M. L. Pool of the Physics Department for many helpful suggestions and criticisms.

2724 Wexford Road
Columbus 12, Ohio

REFERENCES

1. Announcement from Headquarters, Manhattan Project. Availability of radioactive isotopes. *Science*, 1946, *103*, 697–705.
2. Amaldi, E., D'Agostino, O., Fermi, E., Pontecorvo, B., Rasetti, F., and Segrè, E. Artificial radioactivity produced by neutron bombardment. II. *Proc. Roy. Soc.*, 1935, *149*, 522–558.
3. Rotblat, J. Induced radioactivity of nickel and cobalt. *Nature*, 1935, *136*, 515.
4. Sampson, M. B., Ridenour, L. N., and Bleakney, W. The isotopes of cobalt and their radioactivity. *Phys. Rev.*, 1936, *50*, 382.
5. Risser, J. R. Neutron-induced radioactivity of long life in cobalt. *Phys. Rev.*, 1937, *52*, 768–772.
6. Mitchell, J. J., Brown, H. S., and Fowler, R. D. On the isotopic constitution of cobalt. *Phys. Rev.*, 1941, *60*, 359.
7. Livingood, J. J., and Seaborg, G. T. Radioactive isotopes of cobalt. *Phys. Rev.*, 1941, *60*, 913.
8. Nelson, M. E., Pool, M. L., and Kurbatov, J. D. The characteristic radiations of Co^{60}. *Phys. Rev.*, 1942, *62*, 1–3.
9. Deutsch, M., Elliot, L. G., and Roberts, A. Disintegration schemes of radioactive substances. VIII. Co^{60}. *Phys. Rev.*, 1945, *68*, 193–197.
10. Miller, L. C., and Curtiss, L. F., A magnetic-lens electron spectrometer: radiations from 5.3 year cobalt^{60}. *J. Research, Nat. Bur. Standards*, 1947, *38*, 359–364.
11. Evans, R. D. Radioactivity units and standards. *Nucleonics*, 1947, *1*, 32–43.
12. Dunning, J. R., Pegram, G. B., Fink, G. A., and Mitchell, D. P. Interaction of neutrons with matter. *Phys. Rev.*, 1935, *48*, 265–280.
13. Quimby, E. H., Marinelli, L. D., and Blady, J. V. Secondary filters in radium therapy. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 804–818.
14. Stenstrom, K. W., and Marvin, J. F. Ionization measurements with bone chambers and their application to radiation therapy. Am. J. Roentgenol. & Rad. Therapy, 1946, *56*, 759–770.
15. Paterson, R., and Parker, H. M. A dosage system for gamma ray therapy. Part I and Part II. *Brit. J. Radiol.*, 1934, *7*, 592–632.
16. Paterson, R. A dosage system for interstitial radium therapy. Part I. Clinical aspects. *Brit. J. Radiol.*, 1938, *11*, 252–266.
17. Parker, H. M. A dosage system for interstitial radium therapy. Part II. Physical aspects. *Brit. J. Radiol.*, 1938, *11*, 313–340.

CANCER DETECTION CENTERS*

THEIR ROLE IN CANCER CONTROL

By J. ROBERT ANDREWS, M.D.
WEST PALM BEACH, FLORIDA

THE early diagnosis of cancer has been neglected. The enormity of the intellectual effort and the scientific problems involved in the successful treatment of cancer have, in the past, so captivated the interest of physicians that but little attention, until recent years, has been paid to the possibilities for the early diagnosis of cancer. It is, of course, a fact well established that the earlier in the course of the disease a patient with cancer is treated the better are the chances of effecting a cure. This being true the matter of the early diagnosis of cancer assumes an importance at least equal to the problem of its treatment. It is likewise true that once such symptomatic manifestations of cancer as tumefaction, ulceration, hemorrhage or pain impress themselves upon the consciousness of the patient—and it is not until then that the patient, ordinarily, will consult the physician—the cancer may already be incurable. The next logical step is, therefore, the attempt to find cancer in the incipient stage of the disease; that is, before symptoms of the disease have impressed themselves upon the consciousness of the patient. This is the stage which already has been reached by case finding methods in tuberculosis control and this is the stage in cancer control which the cancer detection center program now seeks to attain.

Cancers of certain organs,—the skin, mouth, breasts, uterus and rectum, are readily demonstrable by simple inspection or palpation; cancers of these organs are readily accessible to surgical extirpation or the tissues in which they appear are tolerant to curative irradiation. These, therefore, are the cancers which, because of relative ease of diagnosis, surgical accessibility and tolerance of tumor bed to irradiation, might properly be called the curable cancers and yet the curability of any one group of these cancers, with the exception of cancers of the skin and lip, does not exceed, at present, 35 per cent. If, then, more patients with these so-called curable cancers are to survive, then these cancers, and likewise cancers of other organs, must be found in their incipient stages,—in the stages when, ideally, the curability might be 100, not 35, per cent.

In the absence of a serological or other specific test for either the diagnosis or exclusion of cancer the only case finding method which can be employed is the exhaustive clinical examination of individuals presumably well but desirous of submitting or willing to submit to such examination.

It is these concepts upon which the cancer detection center program is based.

These, or similar concepts, must have been comprehended by L'Esperance[7] when she founded the Strang Cancer Prevention Clinic of the New York Infirmary for Women and Children in 1937 and extended these activities to Memorial Hospital in 1940. Similar concepts must have guided Macfarlane[8] and the group working with her when the Cancer Prevention Clinic in the Women's Medical College of Pennsylvania was founded in 1938. It is interesting to point out that official sanction was given to such a program that long ago by organized medicine as the early work of the Macfarlane clinic was made possible in part by a grant from the Committee on Scientific Research of the American Medical Association. Similar concepts guided Webster[13,14] and the group working with her in founding

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the Cancer Prevention Clinic in the Women's and Children's Hospital in Chicago in 1943. The first large-scale, community-wide effort came, as the result of the interest aroused in these concepts and the impetus given this program by Macfarlane and her group, in 1944 with the establishment, with the approval and under the coordination of the Academy of Medicine of Philadelphia, in the five teaching hospitals in Philadelphia of a series of "clinics" for the conservation of health. Financial support has been given these Health Maintenance-Cancer Prevention Clinics by the Donner Foundation; their number has since grown to ten or more; and their activities and experience have been given wide publicity by their executive secretary Mildred W. S. Schram.[12]

In 1945 the Council on Medical Service and Public Relations of the American Medical Association laid down some rules and objectives for such centers.[11] The clinic or center, as we now prefer to call it, was defined in the following terms: "A cancer detection, cancer prevention, well person clinic is designed to detect abnormalities not producing symptoms sufficient to send the patient to the doctor. These clinics do not diagnose or treat diseases." The Council further recommended that "no such clinics shall be established in any community without the approval of the county medical society." The American College of Radiology approved the cancer detection center program in February, 1946[10] and the American College of Surgeons resolved to inaugurate a program for the survey and approval of cancer detection centers at its meeting in Cleveland in December, 1946.[4]

This concept of the examination of the apparently well for the express purpose of discovering unsuspected cancer has gained wide acceptance in just the past few years and there are now some 120 such centers in twenty-seven states.[3] Sixty-six of these centers, or more than half, are, however, located in only five states. The American Cancer Society has, of course, figured prominently in fostering this concept, in encouraging its wide acceptance, and in financing the detection center programs, the American Cancer Society probably having given financial aid to all of these centers with the exception of the Strang Cancer Prevention Clinics in New York and the Health Maintenance-Cancer Prevention Clinics in Philadelphia.

The interest of organized medicine in Cleveland in a cancer detection center program at the beginning of 1945 was only passive. Active interest was, however, stimulated by the lay members of the Cuyahoga County Division of the American Cancer Society and by the fact that funds of this organization for which commitments had not been made, were available and by the fact that several other groups also were preparing independently to inaugurate such cancer detection centers. Among these other groups was the Elsa U. Pardee Foundation, a private foundation the interest of which is in cancer. In an effort to prevent chaos in such a program and to coordinate the interests and activities of the several groups concerned, the Academy of Medicine of Cleveland,[1] acting through its Committee on Cancer, secured the cooperation of the Cuyahoga Division of the American Cancer Society, the Pardee Foundation, and the Cleveland Hospital Council, which is a voluntary policy forming and purchasing organization of the Cleveland hospitals, to participate in a joint, large scale effort in the organization and operation of cancer detection centers in Cleveland hospitals.

The program is organized according to the scheme shown in Figure 1. It should be emphasized that such a plan of organization might serve as a model for the organization of a similar program in any community where organized medicine, one or more hospitals, and one or more health agencies,—whether they be public, private, or voluntary,—are involved. This is for the very important reason that organization along such lines permits the financial and administrative participation of any number

or kind of health agencies but invests in organized medicine sole authority for the determination of medical policy. In these several respects the Cleveland plan is possibly unique.

In reference to Figure 1, it is apparent that the practicing physicians comprise the membership of the county medical society which in turn functions through committees. The committee on cancer has two functions in the cancer detection center

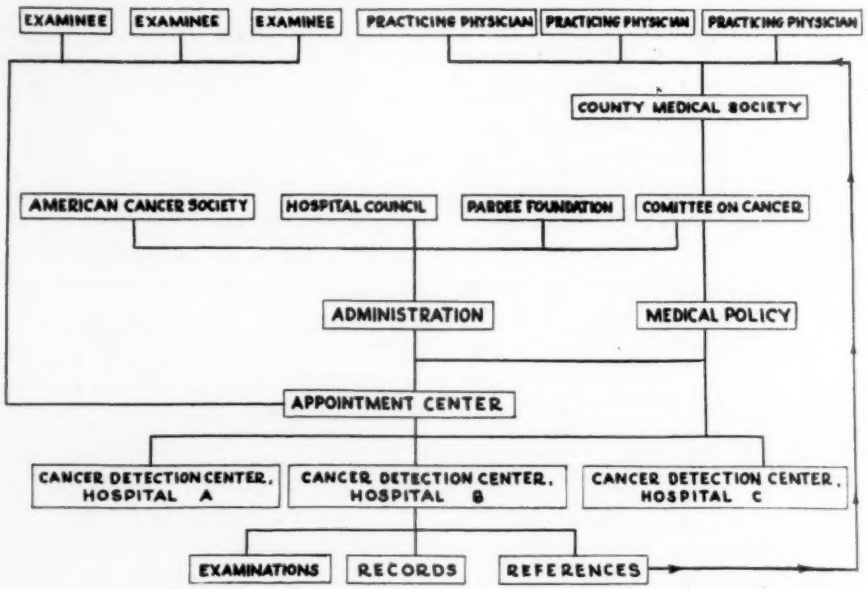

FIG. 1. Organization of cancer detection centers in Cleveland. (Courtesy of the Cleveland Health Museum.)

program. One is cooperative with the other participating agencies,—in this case the American Cancer Society, the Cleveland Hospital Council, and the Pardee Foundation. To this group might be added any number of other agencies, as, for example, visiting nurse associations, other private foundations, or federal, state, or local departments of health. The other function of the committee on cancer is exercised solely and exclusively by it and consists of the formulation and the supervision of medical policy in the appointment center and the coordination of medical policies in the cancer detection centers themselves. The applicant's, or examinee's, first contact with the cancer detection center is through the common appointment center where the applicant is interviewed by telephone in order to determine his or her eligibility for the clinic examination and where an appointment is made for examination at a specific center. The examination is performed by physicians selected by the staff of the hospital in which the center operates and the examination itself conforms to the standards adopted for the program after cooperative study by physician representatives of the several centers meeting with the committee on cancer. These standards are subject to review, modification, deletion, and addition at intervals. The manner in which the prescribed examination is performed is left to the option of the individual clinics. Prescribed records are completed and become the property of the hospital in which the center is located. Examinees in whom abnormalities are found are referred to physicians of their choice with an abstract of the findings of the center. Examinees in whom no abnormalities are found are reassured and invited to make another appointment after six months.

When the program is examined in this fashion it is apparent that it is neither sepa-

rate nor distinct from the practice of medicine as it is known today but is both a part of it and an adjunct to it and that, in the final analysis, the program belongs to the practicing physicians for it is they who comprise the Academy of Medicine. The program is therefore subject to extension, alteration, and even termination by the wishes of these practicing physicians expressed through the Academy of Medicine.

Fifty per cent of the cost of the program is borne by the examinee. The other 50 per cent is borne approximately equally by the American Cancer Society and the Pardee Foundation.

The demands made upon the appointment center for appointments for examinations are in great part dependent upon the publicity given the program. Newspaper publicity of the type used in Cleveland results in such public response that the facilities of the appointment center are overtaxed for several weeks.

CLINIC	ELIGIBILITY		PHYSICIANS REIMBURSEMENT	EXAMINEES FEE	PHYSICAL EXAMINATION		LABORATORY			
	WELL ONLY	ALL	PER PERIOD		COMPLETE	LIMITED	BLOOD	URINE	CHEST X-RAY	VAGINAL SMEAR
1	X		$10.00	$5.00	X		X	X		X
2	X		0 & $5.00	$5.00	X		X	X	X	
3		X	VOLUNTEERS FROM COUNTY MEDICAL SOC.	-0-	X			X		X
4	X		-0-	$5.00	X					X
5	X		VARIABLE	$7.50	X		X	X	X	
6		X	-0-	VOLUNTARY	X					X
7	X		$12.50 (3 HR)	-0-		X*		X	X	X**
8	X		$10.00	$5.00	X		X	X	X	
9	X		-0-	$5.00	X		X	X	X	
10	X		VOLUNTEERS FROM COUNTY MEDICAL SOC.	$7.00	X		X			

* EXAMINATION LIMITED TO N. & T., SKIN, BREASTS, ABDOMEN, PELVIC, RECTAL

** ACTUAL INCISIONAL BIOPSY OF UTERINE CERVIX

Fig. 2. Summary of practices of ten representative cancer detection centers.
Clinic 1: Cancer Detection Clinics of Cleveland.
Clinic 2: Cancer Prevention Clinics of Chicago.
Clinic 3: Milwaukee Cancer Detection Center.
Clinic 4: Los Angeles Cancer Prevention Clinic.
Clinic 5: Strang Cancer Prevention Clinics, New York.
Clinic 6: Kent County Cancer Detection Clinics, Detroit.
Clinic 7: Cancer Detection Center, Johns Hopkins Hospital.
Clinic 8: Tulane University, School of Medicine, New Orleans.
Clinic 9: St. Elizabeth's Hospital, Youngstown, Ohio
Clinic 10: Cancer Detection Center, Grand Rapids.
(Courtesy of the Cleveland Health Museum.)

Figure 2 reviews the practices of ten representative cancer detection centers, Number 1 being the Cancer Detection Centers of Cleveland. Most admit only the apparently well. Physicians are either serving the centers on a voluntary basis or are being reimbursed at a rate of about $5.00 an hour. In most centers the examinee is carrying at least a substantial part of the cost of the

program. The examinations performed in the clinics are routine but tend to be exhaustive in their scope. The amount and character of the laboratory work performed is variable but the usefulness of the Papanicolaou[9] principle of diagnosis of carcinoma of the uterus is gaining wide acceptance.

The character of the prescribed examination justifies more consideration than has heretofore been given it. The tendency in all the centers has been to broaden the scope of the examination. This requires, of course, that more time must be devoted to it which means that fewer applicants can be examined by a given number of physicians or, vice versa, that more physician-hours are required to examine a given number of applicants. In the Cleveland program at the present time two physician-hours are required for the examination of three applicants.

This aspect of the cancer detection center program has certain very important implications. There are only two kinds of examinations which can be performed—and when the term examination is employed the taking of a medical history is implied—the one, the exhaustive, complete examination and the other, the screening examination with the arbitrary elimination of some features of the first type. At first thought, it would appear that the first kind is the only type justified but some consideration of the statistical aspects of the disease cancer and of the problem from the point of view of the preservation of the health of the whole people would suggest that some modification of the examination might properly be made. Study of the statistical incidence of cancer of the male and female (Fig. 3 and 4) shows that cancer of the digestive tract, uterus, breast, genitals (in the male), skin, and mouth comprise 75 to 80 per cent of all cancer. A simple screening examination consisting, then, of a few questions concerning the digestive tract and inspection, palpation, and digital examination of the skin, mouth, breasts, uterus, and the rectum would serve to exclude the great majority of cancers. To this might be added the vaginal smear but other routine laboratory work would not contribute greatly to such a screening procedure. If such a procedure were adopted it is likely that three or more times the number of applicants might be examined per physician-hour than is now possible with the elaborate procedures performed. This means, of course, that a far larger group of the population could have the benefit of such a survey.

Six centers are in operation in Cleveland and at the present rate of examination only a total of 3,600 applicants can be examined in one year.

There are in Cuyahoga County 650,000 persons over the age of thirty. The 3,600 applicants which it is possible for the clinic program to examine at the present rate represent less than 0.6 per cent of the total population over the age of thirty. It costs, at the present rate, $10.30 to examine each applicant in the centers or a total of $37,000 for the year's total number of applicants. It can be predicted on the basis of the present method of screening applicants by telephone that 1 cancer will be found for every 200 applicants examined. The incidence of unsuspected cancer among examinees will vary, of course, depending upon the character of the telephone screening employed and if all applicants are admitted indiscriminately or if applicants are admitted through special agencies interested in cancer the incidence will be very much higher than this. This would anticipate a total of 18 cases of unsuspected cancer discovered this year among the 3,600 examinees of the clinics at a total cost of $37,000, or $2,000 for each case discovered.[2]

When these aspects of any cancer detection center program are studied, and while these statistical aspects may differ in detail from one center to another they will not differ greatly in general, one may logically raise the question whether such an extraordinary expense is justified considering the very limited portion of the population served. These aspects emphasize the need

for giving greater consideration to the type of examination performed in these centers with a view to increasing manifold the number of applicants who can be examined in each physician-hour. In any event the statistical importance so far as the preservation of the public health is concerned.

These considerations have resulted in the disapproval of the cancer detection center program by some county medical societies,

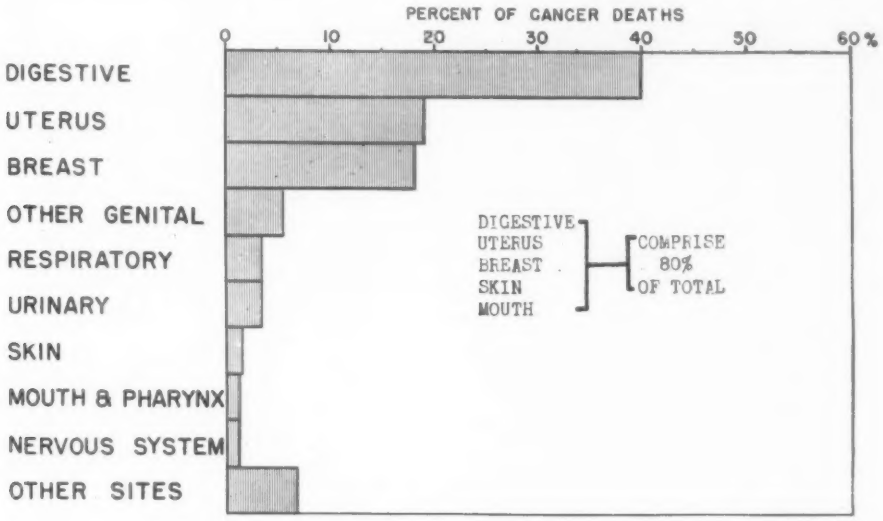

Fig. 3. Percentage of cancer deaths by sites for females. Bureau of Vital Statistics Reports, 1944. (From *Cancer News*, American Cancer Society.) (Courtesy of the Cleveland Health Museum.)

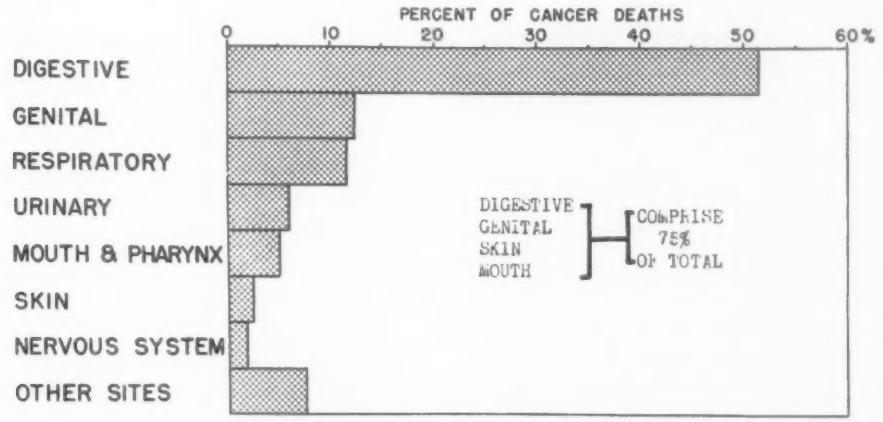

Fig. 4. Percentage of cancer deaths by sites for males. Bureau of Vital Statistics Reports, 1944. (From *Cancer News*, American Cancer Society.) (Courtesy of the Cleveland Health Museum.)

whole cancer detection center program must be viewed as a very luxurious service performed for a fortunate few and for this few the value of the service is inestimable. It is obvious, therefore, that the program as presently constituted and conducted, while of the utmost importance so far as the individual examinee is concerned, is of no the feeling being that the cost is excessive and that, in some instances, the purpose of early diagnosis is defeated by accumulating back-logs of applicants with a waiting list extending several months into the future.[5]

Where economic principles or implications are concerned the relationship between the applicant and the participating

agencies, whether they be public, voluntary, or private, whereby such agencies contribute to the cost of the service performed for the applicant, seems well validated. In the case of the public agency the applicant presumably has contributed to its support by taxation and should therefore be entitled to participate in its benefits; in the case of the voluntary agency the applicant presumably has contributed to its support by gift and is therefore entitled to share its benefits; and in the case of the private agency the express purpose of such an agency may be to give such aid.

This economic relationship beween physicians and the participating agencies is neither so clear nor so valid. The service which the examining physician performs is not experimental; it is an established and skillful procedure. It is a service for which, if it were performed in his own office, he would be well reimbursed. It is a service which no public agency would expect him to perform without adequate reimbursment and neither would he perform it under those circumstances for such an agency. And yet, through custom, the voluntary and private agencies have come to expect that the examining physician himself will participate financially in the program either by volunteering his services or by accepting for them a small honorarium. Reference again to Figure 2 shows that in about half the centers the physicians' services are rendered on a voluntary basis while in no case does the rate of reimbursement exceed $5.00 an hour. It is my opinion, whatever the source of funds,—whether from public, voluntary, or private agencies,—that reimbursement of the participating physician should in all cases be commensurate with the character of the services performed.

If the concept of the cancer detection center is to gain wide acceptance it must be demonstrated that there are certain advantages to such a cooperative program over periodic examinations performed by individual physicians. The one great justification for the program is the perhaps unfortunate fact that the private practitioner has neither the time nor the inclination to perform periodic examinations of the presumably well. The other advantages of the cooperative program over individual initiative have to do with the greater average skill, at least so far as the recognition of cancer is concerned, of the physicians participating in the program, and the greater degree of efficiency, with corresponding reduction of unit cost, which can be achieved by group effort.

Organized medicine is,today, under great stress from many agencies and groups. In the past, organized medicine has tried to remain aloof from such pressure. Organized medicine can no longer, however, categorically and continuously resist and condemn this pressure and the movements initiated by others. The health of the people is the concern of the people. The health of the people is neither solely nor exclusively the prerogative of the medical profession but is the problem of the people itself and therefore of the agencies through which the people act,—federal, state, local, voluntary and private and including the practice of medicine for the latter derives its privileges from, and is responsible to, the people. The concept of the cancer detection center has caught the fancy of the public, and of public, voluntary, and private health agencies to a greater degree than it has appealed to organized medicine itself. The concept, however, must be accepted by organized medicine. The cancer detection center program can be viewed as a clinical research effort—it is not only the laboratory research effort which should have the support of organized medicine—a clinical research effort in the possibilities of the early diagnosis of cancer. Like any other research effort in the field of cancer it may require ten or more years to come to fruit. In the end, it may be found that the chief usefulness of the cancer detection center program was the education of the public and the physician alike to the desirability of periodic examination.

In closing, one might properly quote the words of that distinguished teacher, brilliant scientist, and great humanist, James

Ewing,[6] whose comprehension of the cancer problem in all its aspects was so complete, " . . . there is no room for doubt that the establishment of cancer prevention clinics, while luxurious and somewhat difficult, is one of the best methods for detecting early cancer and precancerous changes. Any community that can establish such an organization would render a valuable service."

1300 No. Poinsettia Avenue
West Palm Beach, Florida

REFERENCES

1. Andrews, J. R. Cancer detection clinic program. *Bull. Acad. Med., Cleveland*, 1946, *31*, 8.
2. Andrews, J. R. Proc. Fifth Annual Health and Welfare Inst. of Cleveland Welfare Federation, Cleveland, 1947.
3. *Cancer News*, American Cancer, Society, 1947, *1*, No. 1.
4. *Cancer News*, American Cancer Society, 1947, *1*, No. 2.
5. Council on Medical Service, American Medical Association, *News Letter*, April, 1947, *4*, 5.
6. Ewing, James. Quoted by L'Esperance.[7]
7. L'Esperance, Elise S. Cancer prevention clinics. *Med. Woman's J.*, April, 1945.
8. Macfarlane, Catherine, Sturgis, M. C., and Fetterman, F. S. Value of periodic pelvic examination in control of cancer of the uterus. *J.A.M.A.*, 1944, *126*, 877–880.
9. Papanicolaou, G. N., and Traut, H. F. Diagnosis of Uterine Cancer by the Vaginal Smear. Commonwealth Fund, New York, 1943.
10. Proceedings of the Board of Chancellors, American College of Radiology, Chicago, 1946.
11. Report of Council on Medical Service and Public Relations of the American Medical Association. *J.A.M.A.*, 1945, *129*, 1209.
12. Schram, Mildred W. S. Organization and results of health maintenance-cancer prevention clinics. *J.A.M.A.*, 1945, *129*, 275–277.
13. Webster, Augusta, and others. A step in cancer control. *Illinois M. J.*, 1945, *87*, 119–126.
14. Webster, Augusta. Periodic physical examination in apparently well women. *Illinois M. J.*, 1947, *91*, 92–96.

CRITERIA FOR REPORTING END RESULTS*

By ELEANOR J. MACDONALD, A.B.†
HARTFORD, CONNECTICUT

THE present day marks the convergence of all trends in cancer to a concentration on the subject, unprecedented in its history. Research in laboratories, in special cancer hospitals and clinics and in general hospitals is going on all over the world. Symposia, international conferences at which leaders in research, diagnosis, therapy and administration report progress, method, and result have demonstrated that although cancer is the problem of every small community, it is also international in its implications. There were more than fifty thousand separate monographs on cancer in the medical literature even before the discovery of Röntgen, and the number since that time has nearly matched the production of nineteen centuries. Yet there are simple facts as to volume, site, incidence and prevalence which are still conjectured rather than specifically known, because no specific criteria for reporting have been established. The different methods of treatment and the end results of the several contributors to this store of information may not be compared except in occasional instances for the same reason.

It has become the practice of many statisticians teaching research methods to students in the medical schools to demonstrate by analysis of papers in current medical journals the requirements of adequate, scientific and literate reporting. It so happens that for the past twelve years the reports of Berven, Martin, Richards and Ralston Paterson have been among patterns I have used as the goal to which the future physicians might well aspire.

The four general criteria for reporting end results are a clear definition of the limits of the anatomic site, a precise statement of the actual time interval involved, a statement of the total number of individuals diagnosed as having cancer of the anatomic site in question in the stated interval of time, whether or not all were treated, and a statement of the actual known status as to presence or absence of the disease of all individuals in the series so that cure and survival rates may be computed. These are self evident and occur to every clinician who studies his results. The many factors which influence end results are so interrelated that unless the disposition of every individual with cancer known to the physician is listed, selection is made at this point, and subsequent students are at a loss in attempting logical comparisons.

From 1936 through 1938 in an effort to obtain the average percentage of five year cures and the percentage of five year cures among the most favorable cases in twenty-eight selected sites, I made a survey of the literature of cancer. Thousands of articles published between 1930 and 1938 were read. Those containing end result figures were abstracted to the following form (Table 1).

No reports were included in which the time interval was uncertain, the number of cases too small, or the results based on less than a five year cure or survival. Four hundred and five separate monographs were abstracted. The range of reported cure rates made any combination of results of different authors hazardous, and the different types of total figure upon which percentages were based made the material difficult to interpret. The survey was useful primarily as a demonstration of the need for consistency in reporting end results, at least net results, regardless of the personal and desirable differences in methods of

* Presented at the Thirtieth Annual Meeting, American Radium Society, Chicago, Ill., June 20–22, 1948.
† Research Statistician, Division of Cancer and Other Chronic Diseases, Connecticut State Department of Health, Hartford, Conn. Consultant in Statistics, Memorial Hospital for Cancer and Allied Diseases, New York City.

presenting the factors influencing these end results.

The high mortality among individuals with cancer has led to the introduction into the statistics of cures and survivals of cancer of a fallacy that is not common in statistics of many other disease entities. An individual treated for cancer and lost to follow up, even though he was clinically free of cancer for several years following treatment is frequently presumed dead of disease and is called a failure. Why it is considered a sound procedure to classify as dead of disease large numbers of individuals who did not continue to report for periodic checks, sometimes after the passage of three, four or more years without symptoms, when it would be considered unsound to call these individuals cured is one of the phenomena which is peculiar to cancer. It follows the theory that to weight results against oneself is to err on the side of accuracy. In the past eight years, in the process of constructing a registry of every individual known to have had cancer in Connecticut since January, 1935, an unusual opportunity to test this theory has come to me. After abstracting every hospital and clinic chart of every patient with cancer in a given institution, and searching for every name in the state Bureau of Vital Statistics from the last date on which that individual was known to be alive to the day of the check, I had a list of names for whom no certificate of death from any cause was filed. I returned to the hospital with this list and prepared letters to the physicians who had treated these patients to ask their cooperation in tracing them and determining their state of health. Connecticut is a small state of under two million inhabitants. Most of the patients lost to follow up were private patients. Fifteen hundred invididuals were found alive, who had been treated for cancer from 1935 through 1940 who, as of 1942, had never been checked clinically by any physician after their initial treatment for cancer. Hundreds of them were presumed dead by the specialists who had treated them. Some of these patients had cancer and eventually died with the disease. Some of them were cures. All of them were brought back under observation, many were treated and were cured of early recurrence of disease. Four individuals who had had colostomies for cancer of the rectum, subsequently had resections of the growths and have been without disease for more than five years. Even in controlled laboratory experiments there are some indeterminate results. Individuals who are lost to follow up without evidence of disease at last medical check are more accurately classified as indeterminate than as dead of disease. The recent world disaster will either cause a large increase in the use of this category, or it will create a literature of purported failures to treatment of individuals whose lives were destroyed before they had a chance to survive successful treatment for the approved period of time.

Following the survey of the literature ten

TABLE I

ABSTRACTS

Author: Title of Article Date Name of Journal Comment not more than two or three lines; e.g., if confused as to total number.	Cases	Five year - cures, selected samples	Five year cures of total cases, not only of operable cases	Five year cures of operable or favorable cases

possible methods of presenting end results were tested. The method recommended by the records committee of the Memorial Hospital was adopted by me as a clear cut way of explaining every contingency that arises in this field. It also is possible by combination to approximate reported results of others. Although all physicians reporting from the Memorial Hospital do not use this form, those who do, subscribe, in so doing, to the minimum criteria for adequate reporting mentioned above. This method of reporting net cures does not prevent an individual reporter from giving details of the factors influencing his end results, but it does give in one table, a concise statement of the disposition of every individual with cancer of a given site known to the hospital, state registry or physician as the case may be. The individual reporter has the breadth of his paper in which to contrast the condition of the individuals he treated with the condition of those who came too late or whose treatment failed. By giving his total experience he is making it possible for others to measure their experience by his, and to know the extent of the problem with which each of them is faced and the comparative results of their therapeutic efforts.

The following table (Table II) from the Connecticut Cancer Record Registry giving the five year end results of the cases of all patients with cancer of the tongue both early and advanced admitted to twenty-nine general hospitals in Connecticut during the years 1935 to 1942, inclusive, will be used to illustrate this method of presenting end results.

There were 200 patients with cancer of the tongue. There were 4 individuals whom we classified as indeterminate as to end result seen in Connecticut in this eight year period. There were no applicants for follow up after treatment elsewhere, who had no evidence of cancer. In almost every series there are usually one or more who fall in this category. There were none with cancer of the tongue who sought consultation only, although this usually does occur because of the proximity of sections of the state to the cancer centers in Boston and New York. There were no patients who refused treatment either for cure or for relief of symptoms. There was 1 patient who died four years after treatment of an accident and who had no recurrence of cancer of the tongue. There

TABLE II

FORM FOR PRESENTING END RESULTS

Five-Year End Results

This series consists of the cases of all patients with cancer of the tongue both early and advanced, admitted to 29 general hospitals in Connecticut during the years 1935–1942*

Total number of patients admitted		200
Indeterminate Group		
Applied after treatment elsewhere, no evidence of cancer on admission or thereafter	0	
Consultation only, no treatment requested	0	
Patient refused proffered treatment or palliation	0	
Dead within five years of other causes, without recurrence of cancer	1	
Lost track of within five years without recurrence of cancer	3	
Total number of indeterminate results		4
Determinate Group		
Total number minus those of indeterminate group		196
Failures		
Dead as a result of cancer	144	
Dead of other causes, cancer present	12	
Living with recurrent cancer	3	
Dead of other causes, unknown whether cancer present	2	
Lost track of with cancer	2	
Lost track of, possibility of recurrent cancer unknown	0	
Total number of failures in treatment		163
Successful Results		
Free from cancer at five years or more		33
Net Five Year End Results		
Successful results divided by determinate group		33/196 = 16.8

* All cases reported as cured have been pathologically proved to have cancer. Lack of pathological proof does not exclude failures.

were 3 individuals who were checked clinically for three and four years but who no longer answered requests that they return for check up. They were not listed as dead of any cause in the state Bureau of Vital Statistics, and all efforts to locate them failed. Because the end result as to cancer was clearly not known in these patients, they were listed in the indeterminate group and were subtracted from the total number of patients when the net five year end results were figured.

Those listed as failures to treatment were the 140 who died directly as a result of cancer, the 12 who died of other chronic degenerative diseases with cancer present, the 3 living with recurrent cancer, the 2 for whom we have death records ascribing death to other causes of whom there is no certain knowledge that cancer was not present, and the 2 who had late cancer when they were lost to follow up. There is often a small number of individuals who drop from clinical observation immediately after initial treatment in whom the possibility of recurrent cancer is not known, and these individuals are listed as failures. Occasionally, after persistent tracing one is found free of disease and the rejoicing is so general that the search for the other untraced patients is carried on with renewed vigor.

Those individuals known without reasonable doubt to be free of disease fall in the classification of successful results. The net five year end results are obtained by dividing the successful results by the determinate group. In this series in Connecticut 16.8 per cent were free from disease at five years. Some of these 33 individuals have been free from disease for twelve years. This is the overall picture in the whole state. Buried in this average is the excellent work of some individual men. The series includes the work of all physicians who diagnosed or treated patients with cancer of the tongue in the hospitals in this state in the time interval stated. As rapidly as the checking and sorting can be accomplished each anatomic site will be reported from the registry in Connecticut according to this method. Differences of opinion may occur as to the desired location for listings under the group headed failures or the cases called indeterminate. If reporters break down their totals in this or even in a more detailed way, by combination one may compare his results with the others.

The greatest source of disagreement with this method lies in the size of the indeterminate group. It is now known from my own experience that it is possible to trace at least 95 per cent of all individuals treated for cancer even when one is faced with the necessity for backtracking fifteen thousand individuals from one to six years after their initial treatment. This was accomplished in Connecticut through effort and remarkable cooperation. Every physician in the state has been written to about at least one individual, and every medical record librarian has demonstrated ingenuity and generosity in searching out former patients. The individuals themselves have shown gratitude at the interest that has been taken in them. More than half the forty thousand individuals recorded in the Connecticut registry were private patients. At no time has the indeterminate group been as high as 10 per cent in any site reported from this registry and usually it is much less than that. At the recent International Cancer Conference in St. Louis, Missouri, several of the men who had exhibits and many of the individuals reading papers had selected this form for reporting their results. A literature is beginning to develop in which, for reports of results of treatment of cancer of a given anatomic site, statistical differences may be figured with assurance, and a cooperative search may be mde for underlying causes for differences discovered in the sincere and constant effort of every physician treating individuals with cancer to improve the prognosis for his patients.

Connecticut State Department of Health
Hartford, Conn.

DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 103 Rutledge Ave.
Charleston, S. C.

THE PREPARATION OF RADON VASELINE OINTMENT

By E. L. HARRINGTON*
University of Saskatchewan
SASKATOON, SASKATCHEWAN

WHETHER or not the radon technician is convinced of the therapeutic value of the radon ointment for use in the treatment of non-healing radiation ulcers he is likely to be called upon to prepare the same. Several rather elaborate methods which employ cylinder-piston combinations have been described, but none as simple nor affording as direct a control of strength as the one herein reported. It has been in use for some time at the radon plant of the Saskatchewan Cancer Commission, located at the University of Saskatchewan and operated by the Department of Physics.

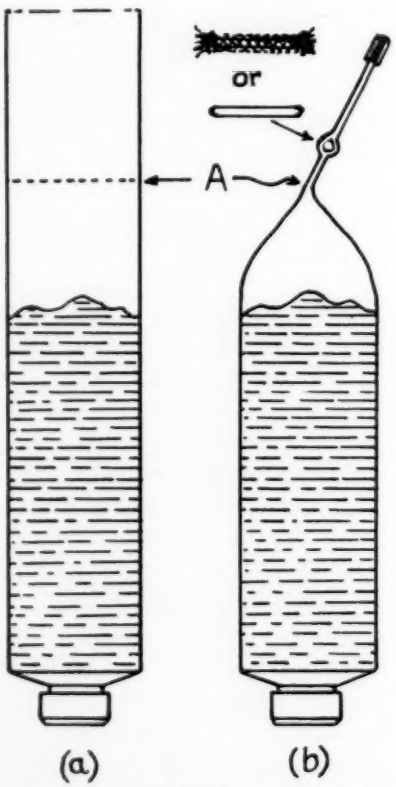

FIG. 1. Collapsible metal tube for containing radon ointment. (*a*) Partially filled, end still open. (*b*) Tube flattened and bent, radon glass capillary introduced, end clamped gas tight, in preparation for breaking glass.

The first step is to introduce the requisitioned quantity of the vaseline or vaseline-lanolin mixture into a standard collapsible metal tube somewhat larger than is required to hold the quantity to be activated. Such empty tubes may be obtained perhaps from a prescription druggist, but certainly from a wholesale drug company. One then prepares a slender glass capillary or "seed" containing the amount of radon needed to give the desired radioactivity to the quantity of ointment being prepared. It is of course rather difficult to get the exact amount desired but if the technician selects a capillary containing slightly more than is required he may reduce the amount by one or more of these methods: altering the length and contents of the capillary, the quantity of vaseline mixture, or the time allowed to elapse before applying the ointment to the patient. One might infer from the literature that the matter of exact strength is not a critical one nor one on which there is any general agreement.

Preparatory to the introduction of the radon one bends, *but without tightly crimping*, the tube just above the mixture as

* Professor of Physics, University of Saskatchewan, and consulting physicist to the Saskatchewan Cancer Commission.

shown by *A* in Figure 1. Above this the capillary tube is inserted and finally the top is closed, tightly crimped and folded to make sure that the end is gas tight. The glass tube is then broken easily since the flexible metal tubing offers little resistance to the slight bending required to break the tube. Care should be exercised to avoid crushing the tube. The bend at *A* should prevent the broken glass from getting into the ointment, but one might prefer to have the capillary tube enclosed in a muslin tube or in a short section of a hollow (braided) string before inserting the tube. In order to expedite the absorption of the radon in the mixture the prepared tube is then lowered into a beaker of water and the temperature raised until its contents are quite fluid. As an indicator of the proper temperature one may use either a thermometer or a test tube containing a small amount of the same mixture. The tube is then shaken sufficiently to ensure a uniform exposure to the radon.

The method described would seem to offer complete control at every stage without any danger of allowing any radon to escape. Also, it requires no special equipment nor difficult technique. The success of the procedure herein described was in part due to the skill and care exercised by the technician, Mr. R. W. Harrington.

University of Saskatchewan
Saskatoon, Sask.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Fiftieth Annual Meeting: Netherland Plaza Hotel, Cincinnati, Ohio, October 4–7, 1949.

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Thirty-first Annual Meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

EDITORIALS

THE FIFTIETH ANNIVERSARY OF THE DISCOVERY OF RADIUM

THE story of radium is at once a romance, filled with picturesque and adventurous scenes which stir the imagination; a drama of great events with the world for its stage, and not without tragedy; and an epic of heroic proportions, which begins in an humble laboratory, assumes a major role in the battle against cancer, reaches a climax in the atomic bomb, and continues into the future with possibilities that no man can foresee.

When the story is written it must begin in the year 1896 with Henri Becquerel, who, acting upon a mistaken hypothesis of Henri Poincare that fluorescence or phosphorescence was the origin of the recently discovered x-ray, was conducting some simple experiments with compounds containing uranium. In the course of these experiments he made the original discovery that uranium emitted rays which could penetrate metallic and other solid objects and which produced effects upon photographic plates like ordinary light. This discovery led directly to the research labors of Marie Sklodowska Curie and her husband Pierre Curie during the succeeding two years. Their patient investigation of uranium ores culminated in December, 1898, in the isolation of a radioactive substance which emitted two million times as much radiation as uranium. They named it "Radium." Their subsequent study of the new substance included both its physical properties and its biological effects. In 1901, Becquerel, who was associated with them in their work, was accidentally burned by a sample of radium which he was carrying in his vest pocket. Soon afterwards Pierre Curie suffered a severe radiation reaction by intentionally applying radium to the skin of his arm. After this the Curies carried out numerous animal experiments to show the biological effects of radioactivity, a term which had been originated by Marie Curie. They are therefore rightly regarded not only as the discoverers of radium but as the pioneers in radium therapy.

In the year 1905 Bergonié and Tribondeau announced their famous law which is the rational foundation of radiation therapy. From that day to the present time radium in some form has been an important weapon in the battle against cancer. The story of its use, sometimes alone, but more often in conjunction with surgery or the roentgen ray, or both, has been fully recorded in the medical literature of the world. On this fiftieth anniversary of its discovery the value of radium for the treatment of cancer and other diseases is well established and its limitations are well known.

We pause to pay tribute to the discoverers and pioneers, but in proportion as we have their faith and vision we will fix our eyes upon the possibilities of progress which are opening up before us in the field of radioactivity. Much has been accomplished already in exploration of the field of the artificially produced radioactive isotopes. It is true that the early optimism concerning their beneficial action in cancer has not been justified. P^{32} causes remissions in leukemia but probably no more effectively than established methods of roentgen treatment. It seems, however, to have proved itself as the treatment of choice of polycythemia vera. I^{131}, because of its concentration in the thyroid gland, seems ideal

for treatment of thyroid cancer but this, too, has been disappointing because the cancer itself exhibits no particular selectivity for the radioactive iodine.

In spite of these unencouraging results progress has been made in establishing the criteria that must be met in the further search for radioactive substances which may be effective in the treatment of cancer. For example, the useful isotope must have a half-life value neither too long nor too short. It must not be so long as to be a menace because of its long retention within the body; it must not be so short as to be relatively inert by the time it is possible to introduce it into the body. Again, only those isotopes which are selectively absorbed by some organ, tissue, or type of cells will be of value for treatment. Na^{24}, which is evenly distributed in the extracellular body fluids throughout the body, offers no possibility for use in the treatment of malignant disease, although it is a valuable tool in medical research.

Research workers throughout the world are eagerly investigating the application of the radioactive isotopes to cancer therapy. A particularly inviting field is the incorporation of radioactive elements into complex organic compounds, nucleoproteins for example. The number of possible compounds in this field would seem to be almost unlimited and the relationship of nucleoproteins to rapid cell division is suggestive of the possibility that a compound may be discovered which would be the vehicle to localize radioactive substances in cancerous tissues.

The dangers in the use of these new radioactive agents must be fully recognized. It is gratifying to know that they are not to be distributed until those in charge of their distribution are satisfied of the adequate training and experience of those who are to use them, and of the provision of proper facilities for their handling and application. Douglas Quick, in the Carman Lecture for 1947, has laid emphasis upon the shortcomings of the method, or lack of method, for the distribution of radium and radon in the United States. He recommends especially the complete integration of radium therapy with therapeutic radiology. The best results are obtained only when the possibilities of roentgen and radium therapy are fully considered and correlated in each individual case. The following brief quotations from his Lecture which is filled with important suggestions are timely in this anniversary year: "Radium fills a place in the field of radiation therapy that, so far, cannot be otherwise provided; unless it is used, and its applications taught, the man in training will never know of those advantages, and the unfortunate patient is apt to become a casualty by omission." . . . "The important feature is to have the radium a part of, and controlled by, the therapy department. It should not be loosely and miscellaneously spread about." . . . "The major responsibility of therapy by irradiation is still directed toward the relief of cancer. It is a serious responsibility. The least we can do is to provide and insist upon a full and complete training before endorsing assumption of such an obligation."

Notwithstanding the wider applicability of the roentgen ray than was the case before high voltages were available, radium continues to occupy an invaluable place in the treatment of cancer. It is vitally important, in every case in which its use is indicated, that it be applied by one who is fully informed of its hazards and who is adequately trained in all that pertains to dosage and methods of application. A fact that is little appreciated by the casual user of radium is that inadequate irradiation, whether because of under-dosage or poor distribution, is quite as harmful as overdosage, since it may result in failure to cure a curable cancer.

Pierre and Marie Curie in their little laboratory in a shed fifty years ago had no intimations of the revolutionary effects of their discovery upon physical science nor of its beneficent role in the treatment of cancer. We of the present generation can

best show our appreciation of their great contribution to humanity by perfecting and extending the use of the agent which they discovered and by pressing forward to new discoveries in the field in which they were the pioneers.

Arthur C. Christie, M.D.

THE ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE fiftieth anniversary of the discovery of radium was celebrated at the recent meeting of the American Radium Society held in Chicago from June 20 to 22, 1948. "The Achievements of Radium in the Fight Against Cancer" was the topic of the Janeway Lecture by Sir Stanford Cade and an address on "Fifty Years of Radium" was delivered by Dr. Edith H. Quimby. The relative position of radium, roentgen rays and surgery in the treatment of cancer was discussed in symposia refresher courses and separate papers. The attendance at the meeting was one of the largest in the history of the Society and the presentations were well received. Important contributions to the program were made not only by representatives of radiotherapy from the United States and Canada but also by the following invited European guests of the Society: Baclesse, Baud and Lamarque of France; Berven of Sweden; Cade, Windeyer and Wood of England, and McWhirter of Scotland.

A symposium was held on "Should Radiotherapy be Separated from X-ray Diagnosis?" Those favoring this move brought forward much more convincing arguments than those opposing the change; they clearly showed the advantage of separation to the cancer patient and to the development of radiotherapy as a whole. The over-all improvement in radiotherapy following separation in some hospitals in the United States, in Sweden and especially in England made it seem inevitable that sooner or later this example will be followed throughout the United States, especially in the larger hospitals.

In the symposium on the "End Results of Treatment of Cancer of the Tongue" a five year follow-up was reported in over three thousand cases from seven outstanding American and European Clinics. Six of the seven speakers chose radium for the primary lesion in the tongue. The French and most British authors advised interstitially placed low intensity radium element needles; whereas Wood and Berven relied chiefly on external radium beam. In addition to the external irradiation, however, Berven electrocoagulated small uncontrolled cancer rests in 80 per cent of his cases. Only Hayes Martin of New York stated that he was reverting to excision, because of disappointment with irradiation of the primary lesion.

The problem of metastasis to cervical lymph nodes was dealt with at the Curie Foundation by routine radical neck dissection in all cases. Wood adjusted the fields of the radium beam for the primary tongue lesion in such a manner as also to include the lymph node bearing area. All other authors treated nodes only when clinically metastatic: When fixed, they were irradiated; when movable, Cade and Windeyer advised resection; Berven treated first by radium beam and resected only if the nodes failed to respond to the irradiation. On the whole, one gained the impression that the majority obtained their best results by interstitial use of radium needles for the primary and radical neck dissection for cervical node metastases.

In the symposium on the treatment of mammary cancer, five year follow-up results were reported in over ten thousand cases. The chief differences of opinion were as to whether simple or radical mastectomy was preferable and whether preoperative and postoperative roentgen therapy was valuable in cases with axillary lymph node involvement. McWhirter was the only one advising simple mastectomy and treatment of the axilla solely by roentgen irradiation: Postoperative roentgen therapy in 513 cases was preceded by radical and in 310 by simple mastectomy; survival was respectively 44.8 per cent and 56.1 per cent. The six other speakers and Adair who opened the general discussion preferred radical

mastectomy; only some of the authors combined this with preoperative or postoperative roentgen therapy or both. Their five year survival figures in cancer limited to the breast varied from 60 to 87 per cent in the different clinics, irrespective of whether or not radical mastectomy was combined with radiotherapy. In cases with axillary metastases, however, the addition of preoperative or postoperative irradiation did seem to make a difference in some of the series where it was used routinely. Thus Cade's figures rose from 29 per cent to 35 per cent when radium was added and Berven quoted 30 per cent when only postoperative roentgen therapy was used and 34 per cent when preoperative and postoperative treatment was given. Windeyer always used postoperative roentgen therapy in this stage of the disease; Taylor in selected cases and Haagensen only when there was microscopic evidence that the operation did not completely remove the cancer.

In evaluating preoperative and postoperative roentgen therapy it is well to bear in mind published information on the efficacy of certain tumor doses as shown by microscopic examination of irradiated tissue and clinical follow-up of cancers of the breast treated only by roentgen therapy. Thus, on microscopic examination of preoperatively irradiated mastectomy specimens, marked radiation damage but not complete destruction of the cancer was noted in 38 patients receiving a tumor dose of 4,500 roentgens in eight weeks. The roentgen therapy was given a few days to one year before radical mastectomy at the Presbyterian Hospital, New York. Clinically, 10 of 32 of the patients with cancer limited to the breast and axilla and treated only by roentgen therapy, remained free from cancer for from seven to eleven years. This result was not obtained, however, until the tumor dosage was raised to 6,000 or 8,000 r in three months. Baclesse's experience at the Curie Institute, Paris, reported at this meeting, was similar. He also did not obtain clinical cures until his tumor dosage in three to four months was 8,000 r or more. McWhirter administered a tumor dose of 3,700 r in two to three weeks. The shorter period of treatment made this dosage more cancerocidal and some growth restraint undoubtedly followed, probably increasing the five year survival rate. It is not likely, however, that this dosage could completely destroy mammary cancer in lymph nodes, nor that it could be as effective as 8,000 r or over given in three to four months. It is difficult to compare McWhirter's statistics with those of the other speakers as the latter separated their operable cases into cases with and without axillary nodes, which McWhirter did not do. We will follow his experiment with interest, but for the present will advise radical mastectomy in cancer limited to the breast and even in those with a single involved node. Haagensen of the Presbyterian Hospital, New York, claims his radical mastectomies have done nearly equally well in both groups. We believe with Haagensen and with Taylor of the Massachusetts General Hospital that improvement in the results of radical mastectomy is more likely to come from stricter selection of cases for this operation than by the routine addition of preoperative or postoperative roentgen therapy. Too many inoperable cases are still operated upon, in the hope that radiotherapy will correct surgical mistakes. It would seem preferable not to operate on these cases but to refer them, after biopsy, solely for treatment with roentgen rays. More vigorous irradiation can then be given and greater growth restraint obtained.

The Refresher Courses, which were an innovation at this meeting and all separate papers were very well received. Refresher Courses will probably form part of future programs. There were discussed the treatment of cancer of the mouth, palate, larynx and pharynx, maxillary antrum, Bartholin gland, cervix, penis, rectum, and melanoma. A preliminary report was given on the use of cobalt^{60} in needles and there were described experimental studies on

comparison of gamma and roentgen rays. Refresher Courses are usually not published. A great many requests were received, however, to have the material mimeographed and sold at cost. This will be done.

This report would be incomplete if we did not mention the help extended by generous friends of the American Radium Society, making it possible to invite the European guests. The intense interest shown by the large audience testified to the appreciation of the presentations.

Maurice Lenz, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

American Radium Society
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Hotels Fairmont and Mark Hopkins, San Francisco, Calif., Dec. 5–10, 1948.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: Chalfonte-Haddon Hall, Atlantic City, N. J., June 5, 1949.

Section on Radiology, American Medical Association
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: 1949, to be announced.

Alabama Radiological Society
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Next meeting time and place of Alabama State Medical Association,

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Brooklyn Roentgen Ray Society
Secretary, Dr. A. H. Levy, 1354 Carroll St., Brooklyn 13, N. Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. George L. Sackett, 10515 Carnegie Ave. Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday of October and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Houston X-ray Club
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Moris Horwitz, 441 No. Camden Drive, Beverly Hills, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Louisville Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 323 Professional Bldg., Charlotte 2, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August. Next meeting Sept. 27, 1948.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Robert M. Lowman, Grace-New Haven Community Hospital, New Haven 11. Meets bimonthly second Thursday, at place selected by Secretary.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting Jan. 7–8, 1949, Fort Worth, Texas.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. Ivan J. Miller, 49 Fourth St., San Francisco 3. Meets monthly on third Thursday at 7:45 P.M., January to June at Lane Hall, Stanford University Hospital, and July to December at Langley Porter Clinic, University of California Hospital.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

British Empire

British Institute of Radiology Incorporated with the Roentgen Society
Medical Members' meeting held monthly on third Friday at 2:30 p.m. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 2100 Marlowe Ave., Montreal 28, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 p.m.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano Torino, Italy. Meets biannually.

LOS ANGELES RADIOLOGICAL SOCIETY

The first annual Mid-Winter Radiological Conference sponsored by the Los Angeles Radiological Society will be held at the Biltmore Hotel, Los Angeles, California on Saturday and Sunday, February 26 and 27, 1949. All of the courses will be given by prominent Pacific Coast radiologists. At the Biltmore Hotel on Saturday evening, February 26, a banquet will be held preceded by cocktails. The main speaker of the evening following the banquet will be Dr. Frederick E. Templeton of Seattle, Washington, whose subject will be "The Differential Diagnosis of Benign and Malignant Gastric Lesions." Reservations and information concerning the meeting can be obtained by writing to Dr. Donald Laing, 75 North Madison Avenue, Pasadena 1, California. Fifteen dollars is the fee for the entire two day session.

NORTH CAROLINA RADIOLOGICAL SOCIETY

The North Carolina Radiological Society held its October meeting in conjunction with the Matheson Foundation Medical Lectures in Charlotte, North Carolina, on October 22, 1948. During the morning session an hour was devoted to a Film Reading Session in which the following guests participated: Dr. Paul C. Swenson, Dr. Robert J. Reeves, Dr. J. P. Rousseau and Dr. E. P. Pendergrass. A paper entitled "Problems in the Diagnosis of Diseases of the Large Intestine" was given by Dr. Paul C. Swenson, Professor of Radiology, Jefferson Medical School, Philadelphia.

ANNUAL LIPIODOL AWARDS FOR 1948

Roentgenologists from all sections of the country submitted examples of diagnostic roentgenograms in the Annual Lipiodol Awards program for 1948. The technical excellence of the many entries offers further evidence of the great progress achieved in this specialty.

Awards were made to roentgenologists in four categories of roentgenography. Entries submitted were judged for the extent of diagnostic features revealed and general technical excellence of roentgenograms in otolaryngology, bronchography, uterosalpingography and the delineation of sinus tracts. The six roentgenologists receiving awards were: otolaryngology—Dr. Henry M. Scheer, New York; bronchography—Dr. J. A. Crellin, Philadelphia, and Dr. Louis Schneider, New York; uterosalpingography—Dr. A. P. Echternacht, Crawfordsville, Indiana, and Dr. B. S. Epstein, New York; sinus tracts—Dr. Sidney E. Foster, San Francisco, and Dr. B. S. Epstein, New York.

Entries were reviewed by a distinguished board of judges consisting of Dr. Lawrence Reynolds, President of the American Roentgen Ray Society; Dr. Ira H. Lockwood of Kansas City, Missouri, and Dr. Irving Schwartz of New York.

EXECUTIVE COUNCIL AWARDS AMERICAN ROENTGEN RAY SOCIETY

The Awards (First Award, $500.00; Second Award, $300.00) are granted for original, unpublished, scientific contributions prepared by candidates for admission to membership in the American Roentgen Ray Society and considered worthy of the Awards by the Executive Council. It is understood (a) that one, both, or neither of the Awards need be granted in a given year; (b) that the candidate receiving the Award must be elected to membership in the Society; and (c) that a suitable certificate accompany the Award.

Vol. 60, No. 6

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

Department Editor: George M. Wyatt, M.D., 1835 Eye St., N.W., Washington 6, D. C.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

Cappon, D.: Intracerebral calcification in a microcephalic 850
Pennybacker, J.: Cerebellar abscess 850
Phillips, G.: Primary cerebral hydatid cysts .. 850
Ingraham, F. D., Bailey, O. T., and Barker, W. F.: Medulloblastoma cerebelli 850

Neck and Chest

Ward, R.: Cancer of the thyroid 851
Kjellberg, S. R.: A previously unreported sign of foreign bodies in the trachea 852
Nielsen, K.: A case of multiple tracheal diverticula 852
Maurer, E., and DeStefano, G. A.: Eosinophilic granuloma of rib 852
Lloyd, M. S.: Tumors of the anterior mediastinum 852
Soleman, W. A.: Pulmonary heart disease 853
Gubergrits, A. Y.: Occult injuries to the heart 853
Thomas, S. F., and Garland, L. H.: Roentgen cardiac kymography 853
Wald, B.: Contributions on the roentgenology of the left auricle 854
Singer, J. J.: Bronchiectasis 854

Skeletal System

Schleicher, E. M.: Miliary tuberculosis of the bone marrow 854
Knutsson, F.: Two synovial fibrosarcomas (Jönsson) 854
Westerhorn, A.: Marrow nailing of recent fractures, pseudarthrosis, and bone plastic experience in 100 cases 855
Colson, G. M., and Willcox, A.: Phalangeal metastases in bronchogenic carcinoma 855
Lennon, W., and Chalmers, Isabella: Ankylosing spondylitis 856

Blood and Lymph System

Symmers, D.: Lymphoid diseases 856
Gardner, L. B.: Cooley's erythroblastic anemia in two Chinese boys 856
Prinzmetal, M., Ornitz, E. M., Jr., Simkin, B., and Bergman, H. C.: Arterio-venous anastomoses in liver, spleen, and lungs 857

General

Cone, R. B.: Review of Boeck's sarcoid with analysis of twelve cases occurring in children 857
Schwartzman, J., Maffia, A., Crusius, M. E. and Brunhoffer, A.: Congenital toxoplasmosis 857
Stout, A. P.: Mesenchymoma, the mixed tumor of mesenchymal derivatives 858

ROENTGEN AND RADIUM THERAPY

Graham, V. P., and Meyer, R. R.: Experiences with nasopharyngeal carcinoma 858
Laing, D. R.: The roentgen treatment of subacute sinusitis in children 858
Beckstrand, G.: Palliative procedures in advanced cancer of the mouth 859
Erskine, A. W.: The management of advanced cancer of the breast 859
Costolow, W. E.: Care of patients with advanced pelvic cancer 859
Pund, E. R., Nettles, J. B., Caldwell, J. D., and Nieburgs, H. E.: Preinvasive and invasive carcinoma of the cervix uteri 860
Drips, Della G.: Ovarian dysfunction in young women treated with low-dosage irradiation 860
Johnston, J. R., and Jacox, H. W.: Rectal hemorrhage following irradiation for carcinoma of cervix 861

MISCELLANEOUS

Graef, I., Karnofsky, D. A., Jager, V. B., Krichesky, B., and Smith, H. W.: Clinical and pathologic effects of nitrogen and sulfur mustards in laboratory animals 861
Mallet, L.: Counter for ionizing particles 862

ROENTGEN DIAGNOSIS

HEAD

CAPPON, D. Intracerebral calcification in a microcephalic. *Lancet*, May 22, 1948, *1*, 795.

This is an incomplete case study of a nine months old female microcephalic Eurasian. Clinically the child was listless and backward. The chief interest centers around the roentgenogram of the skull which is well reproduced and presents a very unusual symmetrical calcification thought to be in the walls of grossly dilated lateral ventricles. Infantile toxoplasmosis is suggested as a possible diagnosis.—*J. S. Summers, M.D.*

PENNYBACKER, JOE. Cerebellar abscess; treatment by excision with the aid of antibiotics. *J. Neurol., Neurosurg. & Psychiat.*, Feb., 1948, *11*, 1–12.

In a series of 100 brain abscesses in the past nine years, 18 were cerebellar and, with one exception, all were due to mastoid infection. Of the first 9 cases, only 2 survived. Of the last 9 cases, 8 recovered.

Increased recovery of the latter group was directly referable to instillation of penicillin into the abscess cavity.

The author states that roentgenograms of the skull were of no particular help in diagnosis of cerebellar abscess other than to show the presence of a mastoid infection. On the other hand, instillation of thorotrast and penicillin into these abscess cavities following aspiration was of considerable help in judging the size of the abscess and therefore progress in healing. For example, if an abscess does not demonstrably reduce itself over a reasonable period of time as demonstrated by thorotrast, total excision is to be contemplated.—*Russell R. Jauernig, M.D.*

PHILLIPS, GILBERT. Primary cerebral hydatid cysts. *J. Neurol., Neurosurg. & Psychiat.*, Feb., 1948, *11*, 44–52.

Preoperative diagnosis of a primary cerebral hydatid cyst is uncommon even in a country (Australia) where hydatid cyst is relatively common. Symptomatology usually implies only the presence of a space-occupying lesion causing increased intracranial pressure; however, the disease should be suspected in such a picture seen in a child referred from a sheep-raising district. If one is not aware of this possibility, the intracranial field may be sprayed with scolices through performance of a ventriculogram or improperly planned operation. Therefore, if hydatid cyst is suspected, air studies should not be carried out and localization should be made from the clinical picture. There is no objection to following the postoperative course with encephalograms after the cyst has been completely removed.—*Herbert Lobsenz, M.D.*

INGRAHAM, F. D., BAILEY, O. T., and BARKER, W. F. Medulloblastoma cerebelli; diagnosis, treatment and survivals, with a report of 56 cases. *New England J. Med.*, Feb. 5, 1948, *238*, 171–174.

In 1925 Bailey and Cushing described medulloblastoma cerebelli as a midline cerebellar glioma of childhood characterized by rapid growth, abrupt onset of increased intracranial pressure, and cerebellar dysfunction. It is now well known that medulloblastomas are far better treated by irradiation than by radical surgery, but the optimum radiation dosage and the role of surgery remain to be more precisely evaluated.

Fifty-six patients with histopathologically verified medulloblastoma cerebelli, seen at the Children's Hospital (Boston) and the Peter Bent Brigham Hospital since 1930, were reviewed. Eighteen were in the first five years of life; 24, in the second five years. However, typical tumors were seen in patients as old as thirty-seven and sixty-five years.

Although 41 tumors occupied the classic midline cerebellar location, 10 were in the pons and pontine angle, and 5 were in the cerebellar hemispheres. The average age of patients with midline and hemisphere tumors was 7.5 years; that of the pontine and angle tumors, 16.1 years.

Symptoms had been present for an average of three months before hospitalization. While the clinical picture is usually characteristic, benign or radioresistant posterior fossa tumors may mimic the pattern often enough to make biopsy important before roentgen therapy is begun.

Posterior fossa exploration was carried out in 53 cases. Surgical measures consisted of biopsy, removal of tumor bulk if convenient, and re-establishment of cerebrospinal fluid drainage when necessary by a Torkildsen tube in children, or by third ventriculostomy in adults.

Nineteen cases showed characteristic extension to subarachnoid spinal and cerebral pathways. Those with spinal metastases usually showed cord symptoms, including segmental pain, cord bladder, paraplegia, or Horner's syndrome.

Seven of the 56 patients survived three years; only 3 of the 7 survived five years; 1 patient still living twenty-two years after her original admission. Analysis of survival according to type and amount of treatment shows the marked effectiveness of roentgen therapy in prolonging life and affording comfort in this extremely malignant tumor. Seventeen patients received no roentgen therapy, with an average total survival time of 0.3 months. Six received an undetermined amount of roentgen therapy, with an average survival of 7.4 months. Nine received 150–2,850 r, with an average survival of 7.6 months. Fifteen received 4,500–9,600 r, with an average symptom-free interval of 24.0 months, and average survival of 31.6 months. Nine received 10,800–30,000 r, with an average symptom-free interval of 44.6 months, and average survival of 54.0 months. The authors emphasize that although the larger doses of radiation may be assumed to be the cause of the longer survival, it is also true that only those patients who lived a relatively long time after admission could accumulate the large doses.

Leukopenia occasionally required interruption of treatment. Most patients suffered from post-therapy vomiting, and 1 died of acute cerebral edema after one treatment of 150 r. Despite the large doses given (up to 30,000 r to the skull and spine over three and a half years), no degenerative changes in the central nervous system were observed.

The authors conclude that the present management of choice begins with immediate exploration as soon as the diagnosis of posterior fossa tumor is made, in order not to jeopardize the vision of children who have a benign cerebellar tumor. The tumor is biopsied at operation, and a larger portion of the tumor resected if possible, and a means for circulation of cerebrospinal fluid is provided if necessary. As soon as the wound has healed, the patient is given intensive radiation therapy to the skull and spine, to a dose of approximately 5,000 r. The cerebellar portals are given an additional course in six months, sooner if necessary. Reexploration is indicated if obstruction to cerebrospinal fluid drainage appears or recurs; a Torkildsen tube is used in younger patients, but a third ventriculostomy may be effective in adults.—*Henry P. Brean, M.D.*

NECK AND CHEST

WARD, R. Cancer of the thyroid. *California Med.*, March, 1948, *68*, 170–172.

The classic signs of advanced thyroid cancer —rapid growth, fixation, hoarseness, and dysphagia—are signs of impending death. Recognition of early cancer of the thyroid, however, is difficult, and often impossible by clinical means. Carcinoma is not common in diffuse toxic goiter, or in diffuse non-toxic thyroid enlargements of adolescence or pregnancy. In nodular goiters, on the other hand, malignancy is common, particularly in men, in children, or where the nodule is solitary. More than 20 per cent of nodular goiters in children under fifteen may be malignant. In adults, about 5 per cent of clinically benign nodular goiters prove to be malignant on pathological examination, and the percentage is much higher if the thyroid mass is solitary. In men, more than 10 per cent of multinodular goiters prove to be malignant, although nodular goiter is six to ten times more frequent in women. In a large clinic series, there was 1 cancer in each 8.3 males with nodular goiter, and in another series 1 malignancy to each 6 male patients.

Since the prognosis for cure and survival is highest for those patients in whom malignancy is discovered only on pathological examination, and lowest for those in whom malignancy is already suspected clinically, surgical removal should be advised for those patients with nodular goiter who fall into the groups with relatively high likelihood of malignancy. These are the solitary nodules, nodular goiters in men, and nodules in children.

One is therefore justified in advising operation for all men with nodular goiters; for all patients, male or female, with solitary tumor of the thyroid; for all children with nodular goiter; and for all patients who show recent increase in size, pressure symptoms, or dysphagia in long-standing nodular goiters.

Surgically, the nodule should not be simply enucleated, but the involved lobe should be excised. If biopsy shows a papillary carcinoma, the bulk of the tumor should be removed, followed by roentgen therapy. If anaplastic malignancy is demonstrated, the author is

pessimistic over the possibility of cure, doubting the value of radical operation and questioning the value of even palliative irradiation. The presence of discrete lymph node metastases, however, should not in itself contraindicate an attempt at surgical and radiotherapeutic cure, as these are often papillary carcinomas responsive to roentgen therapy.—*Henry P. Brean, M.D.*

KJELLBERG, SVEN ROLAND. A previously unreported sign of foreign bodies in the trachea. *Acta radiol.*, 1948, *29*, 300–302.

If a non-radiopaque foreign body is present in the trachea and the usual signs of bronchostenosis are lacking or are uncertain or insignificant, the roentgenological diagnosis then becomes much more difficult. In such cases a sign which depends on the softness of the tracheal cartilaginous rings in small children can be of great help. If a foreign body is lodged in the trachea, on inspiration the trachea below the foreign body becomes considerably dilated, especially the larynx and pharynx. On expiration, the lower portion of the trachea, on the contrary, either widens slightly or returns to normal width, while above the foreign body, the air passages become of normal or possibly narrower than the normal width.—*Mary Frances Vastine, M.D.*

NIELSEN, KAREN. A case of multiple tracheal diverticula. *Acta radiol.*, 1948, *29*, 331–334.

Tracheal diverticula can be divided in the following groups:

1. Those which are supposed to be congenital. They are always situated on the right side of the trachea at the site of the tripartition of the bronchial tree. They always extend obliquely down and outwards and are shaped like a short cylindrical tube. It is presumed that they are rudimentary bronchi.

2. Flask-shaped diverticula which usually have a narrow inlet. These are usually found in the middle third of the trachea to the right at the junction of the cartilaginous and membranous portions. Usually they are small and are often multiple. As a rule, they contain a viscid mucus. This type has never been found in children. They probably result from the retention of mucus in the paratracheal glands or from increased intratracheal pressure.

3. Diverticulum-like groove-shaped protrusions of the posterior tracheal wall. These diverticula are delimited by transverse crescent-shaped mucous membrane folds connecting the ends of the cartilage posteriorly. The trachea is usually dilated. There is atrophy of the elastic muscular tissue. These diverticula are usually seen in adults who have suffered from chronic respiratory tract diseases.—*Mary Frances Vastine, M.D.*

MAURER, ELMER, and DESTEFANO, GEORGE A. Eosinophilic granuloma of rib. *J. Thoracic Surg.*, June, 1948, *17*, 350–356.

Solitary eosinophilic granuloma may simulate bone cyst, giant cell tumor, Ewing's tumor, solitary myeloma, osteogenic sarcoma and osteomyelitis. Multiple lesions may present the same findings as multiple myeloma, metastatic tumor, osteitis fibrosa cystica, Letterer-Siwe disease and Hand-Schüller-Christian disease.

Approximately 39 cases of eosinophilic granuloma have been reported to date. Only 6 of these lesions have been solitary in the rib. The following case of a sixteen year old boy with a clinical history and roentgenologic findings consistent with osteogenic sarcoma is reported. Pain in the left chest was the only symptom complained of. A destructive, expansile process involving the posterior 9 cm. of the fifth rib on the left was seen on the roentgenogram. Pleural thickening about the lesion was noted. This seemed to favor an infectious process, such as osteomyelitis, while the bone destruction and expanding character of the tumor suggested a primary rib sarcoma. Giant cell tumor was also considered in the differential diagnosis. The diagnosis of eoisnophilic granuloma was made from the surgical specimen removed.

The roentgenographic appearance, pathology, treatment and prognosis of eosinophilic granuloma is discussed.—*Frederick M. Reis, M.D.*

LLOYD, MILTON S. Tumors of the anterior mediastinum; report of six cases. *Dis. of Chest*, May-June, 1948, *14*, 396–414.

The author reports in detail with roentgenograms of 6 cases of which 5 were treated surgically. These included 3 teratomas, one each lipoma, lymphangioma, and "undifferentiated" tumor of newborn. The importance of roentgen examination for early diagnosis is stressed, as well as prompt surgical intervention before the

cysts become infected or ruptured.—*Fred R. Gilmore, M.D.*

Sodeman, W. A. Pulmonary heart disease. *Dis. of Chest*, May-June, 1948, *14*, 360–365.

The author collected 123 cases of cor pulmonale for analysis of pulmonary hypertension due to pulmonary disease per se: 75 cases of emphysema, 14 bronchial asthma, 9 tuberculosis, 8 silicosis, 7 bronchiectasis, and 5 silicotuberculosis. These conditions cause a change in the alveolar pressure so as to increase resistance of blood flow to the lungs. The pulmonary fibrosis, compensatory polycythemia, and overfilling of the heart are secondary aggravating factors. The clinical picture is described with distended neck veins, hepatomegaly, prolonged circulation time, and dependent edema, as well as dyspnea, cough, and hemoptysis. Cyanosis is a serious sign of early failure. The usual studies involve electrocardiogram, hemodynamics, and other laboratory procedures. Roentgenographic and fluoroscopic evidence of right ventricle enlargement with prominent pulmonary conus may be seen on the oblique views long before other evidence of cardiac enlargement. Only 4 of 15 cases with a single posteroanterior film showed suspicious evidence of cor pulmonale.—*Fred R. Gilmore, M.D.*

Gubergrits, A. Ya. Occult injuries to the heart. *Am. Rev. Soviet Med.*, Dec. 1947–Jan. 1948, *5*, 61–63.

This communication deals with 26 cases and consequences of lodged foreign bodies in the heart. Splinters were localized in the great vessels in 2 cases and in the cardiac musculature in 24 cases. In no case was the foreign body found in the cavities of the heart.

The author feels that fluoroscopy is the diagnostic method of choice in foreign body injuries of the heart and it is superior to roentgenography. It should be performed routinely, slowly turning the patient about an axis of 360°. It is essential to determine whether the foreign body is situated within a cavity, or in the wall, or whether it lies near the cardiac shadows. If it lies in the muscle or near the cardiac shadow the splinter shows movements synchronous with systole and diastole. If the foreign body lies in one of the heart cavities it makes whirling movements as a result of the blood current. Such cases have been reported. There may be very little reduction in the working capacity of these patients.

In most cases no absolute indication exists for removal of a metal splinter from the heart. Surgical intervention may be justified when a purulent infection occurs in the area of the foreign body or when a beginning migration implies danger.—*R. A. Butz, M.D.*

Thomas, S. F., and Garland, L. H. Roentgen cardiac kymography; electrocardiographic correlation. *California Med.*, March, 1948, *68*, 126–129.

Introduction of single slit roentgen kymography by Sabat in 1911, and perfection of the multiple slit method by Stumpf in 1928, have made available a technique for permanently recording the pulsations of the heart and great vessels. In order to evaluate one aspect of the reliability of roentgen kymography in diagnosis, the authors correlated the kymographic findings of 249 cases with the electrocardiograms.

Using a conventional kymograph with multiple 0.4 mm. slits and a film excursion of 12 mm., exposures of $1\frac{1}{2}$ to 2 seconds were made in mid-inspiration at as near neutral respiratory pressure as possible. Criteria for kymographic diagnosis of myocardial abnormality included decreased height of wave, sharpening or splintering of peak, and suppression or paradoxical reversal of local movement.

Average age of the cases was thirty-eight years; for those with a clinical diagnosis of coronary artery disease or hypertension, it was 44.5 years. The group comprised patients with suspected or known cardiac disorder, ranging from functional disturbances to myocardial infarction.

Roentgen kymographic and electrocardiac diagnoses correlated well in 80.5 per cent of the cases, or 201 patients. In this group, both methods were positive in 11.3 per cent, negative in 58.4 per cent, and questionable in 10.8 per cent. There was failure of correlation in 48 cases, or 19.5 per cent. Twenty of the failures were unequivocal disagreements, and probably represent inherent error in either method of examination. In the other 28 cases of lack of correlation, one of the methods was questionable while the other was positive or negative, and the lack of correlation therefore not clear-cut. The authors point out that, if it is assumed the findings in this last category of uncertain correlation may still have been of clinical value

in arriving at a diagnosis, the over-all figures result in an error of less than 10 per cent.

Kymograms of 4 illustrative cases are shown, 1 demonstrating a pathologically verified myocardial infarct in which the electrocardiogram was negative. Films of two other myocardial infarcts, and of a stab wound of the heart, are also presented.

Properly interpreted roentgen kymograms, therefore, are a reliable source of information supplementing clinical and conventional roentgenologic methods. Occasionally they provide data not obtainable clinically or electrocardiographically. Roentgen kymograms may supply important diagnostic information in suspected myocardial disease when the electrocardiogram is inconclusive or even negative.—*Henry P. Brean, M.D.*

WALD, B. Contributions on the roentgenology of the left auricle. *Acta radiol.*, 1948, *29*, 335–342.

Direct roentgenological representation of the posterior wall of the left auricle cannot be afforded because this portion of the heart has no surface of contact with the air-containing lung. The author demonstrates by both anatomic and roentgenological investigations that the outline of the heart shadow on the right, when confined to the right anterior oblique position, is always formed by the right auricle and not by the left one. The upper portion of the right border of the heart shadow may protrude in the right anterior oblique position should pathological enlargement of the left auricle occur. Such protrusion is caused not by alterations in the posterior wall of the left auricle but by expansion of the heart directed ventrally and to the right.—*Mary Frances Vastine, M.D.*

SINGER, JACOB J. Bronchiectasis. *Dis. of Chest*, Jan-Feb., 1948, *14*, 92–106.

The author outlines the salient features of bronchiectasis. The most common etiological agents are nasal sinus disease associated with pulmonary findings, and silicosis. It is classified in two forms; congenital, and acquired bronchiectasis. The first is noted with cysts, and congenital malformations, while the second usually follows exanthomatous diseases, foreign bodies, and tumors. The clinical symptoms of cough, expectoration, and hemoptysis are correlated with the pathological processes. The role of roentgen diagnosis is stressed in differentiating the various bronchiectatic dilatations: grape, clubbing, cylindrical, saccular, and bead formation. The author outlines various methods of bronchography using iodized oil and warns of the infrequent allergy, iodism, which usually subsides in several days, and the rare atelectasis due to an oil-blocked bronchus. He concludes the modern medical and surgical treatment by stating that the only effective cure is surgical removal of the diseased portion of lung.—*Fred R. Gilmore, M.D.*

SKELETAL SYSTEM

SCHLEICHER, EMIL MARO. Miliary tuberculosis of the bone marrow. *Am. Rev. Tuberc.*, Feb., 1946, *53*, 115–121.

Data derived from postmortem material and from terminal and known cases of pulmonary and generalized miliary tuberculosis showed that tuberculosis affects the bone marrow frequently enough to justify the use of the sternal aspiration method as a means of detecting the disease early. The use of a standard sternum needle makes the method a simple and safe procedure. The author has not observed any serious injury to the bone. Serial aspirations can be done at short time intervals without great discomfort to the patient. Thus the possibility is open to obtain information with respect to the course of the disease and by the same token the effectiveness of chemotherapeutic agents may be studied in man. Aspirated sternal marrow can be directly innoculated into a guinea pig, cultured, imprinted or smeared on a glass slide for the demonstration of the tubercle bacillus.—*James J. McCort, M.D.*

KNUTSSON, FOLKE. Two synovial fibrosarcomas (Jönsson). *Acta radiol.* Jan., 1948, *29*, 4–6.

In his doctor's thesis Jönsson has clarified the nomenclature of malignant tumors arising in joint capsules, tendon sheaths, and bursas. He divides these malignant synovial tumors into two different groups, namely synovialomas and synovial fibrosarcomas. These two kinds of tumors show both clinical and micro-anatomical differences. The synovialomas are more malignant and often metastasize to the regional lymph glands, the lungs and internal organs. The synovial fibrosarcomas, on the other hand, very seldom metastasize to the lungs and other

internal organs. The synovialomas, as distinct from the fibrosarcomas, are very responsive to roentgen treatment.

The fibrosarcomas sometimes contain calcifications causing them to have a roentgen diagnostic interest. The author describes 2 cases of synovial fibrosarcoma. In the early stages, the synovial fibrosarcoma is usually interpreted as an inflammatory process. There is extreme tenderness but no spontaneous ache. Surgical intervention and roentgen treatment are necessary. There is a risk of local recurrences and remote metastases.

In his 2 cases, the author could ascertain the diagnosis through the characteristic calcification. The calcifications consisted principally of sharp-edged shards which proved they were part of the tumor structure. Calcium precipitation in a necrotic tissue would have a more uncharacteristic, amorphous appearance.—*Mary Frances Vastine, M.D.*

Westerhorn, Anders. Marrow nailing of recent fractures, pseudarthrosis, and bone plastic experience in 100 cases. *Ann. Surg.*, April, 1948, *127*, 577–591.

In this excellent paper the relatively new method of fixation of long bone fragments by intramedullary nailing is well demonstrated with the apparatus used and with illustrative cases for each type of orthopedic problem it best serves. The author is very encouraged with his results. In his opinion it represents an important advance in treatment of fractures of the femur as nailing of hip fractures. The intramedullary nails are made of stainless steel of several widths and ranging in lengths from 10–45 cm. The nails are thin and V-shaped but of good quality steel so although flexible they will not bend. The advantages of this construction permit firm fixation in the marrow cavity and minimum involvement of the marrow and endosteum by the nail surface. Special tools are required for both the insertion and removal of these nails.

In fractures of the femur the nail can be inserted directly through the soft bone of the upper surface of the greater trochanter. However, in the humerus, radius, ulna and tibia a small hole must be made in the cortex some distance from the fracture site. In the actual procedure it is essential to have close apposition of the fragments to permit direct threading of the nail from one portion of the medullary cavity to the next. Empirically it was found best to use a leader in the form of a Kirschner wire. This is done under fluoroscopic control or using multiple films. In judging the size of the nail to use, at 75 cm. focal distance the marrow is actually 1 mm. smaller than it appears on the roentgenogram. Although the marrow cavity of the femur is symmetrical it has been found that the central portion of the tibial marrow cavity is the narrowest so in fractures of the proximal and distal thirds of the tibia firm fixation is difficult to obtain. The dangers of intramedullary nailing include marrow destruction, fat embolism and osteomyelitis. Actually there is little marrow damage and the nails are removed once the fracture is solid. Fat embolism has not definitely been proved to result from the nailing procedure or the fracture site itself. To date the experience with infection has been unusual in that the patients with open wounds have done well with naiiing. In those cases where the nail was removed because of osteomyelitis the infection became worse. The author believes the nail permits the pus to drain off.

The advantages of intramedullary nailing in fractures and pseudarthrosis are: (1) very firm fixation of the fragments with close apposition, (2) shortened bed stay, (3) early weight bearing, (4) reduced pain, and (5) less in the way of secondary change due to long immobilization, i.e., stiff joints, muscular atrophy and circulatory disorders.—*T. D. Allison, M.D., and C. L. Hinkel, M.D.*

Colson, G. M., and Willcox, A. Phalangeal metastases in bronchogenic carcinoma; report of three cases. *Lancet*, 1948, *1*, 100–102.

This is a report of 3 cases seen at the Middlesex Hospital. In all 3 cases the phalangeal metastases closely resembled, clinically, an inflammation and were at first assumed to be a paronychia, Whitlow or infected bunion. Roentgenography revealed the true nature of the lesion and biopsy confirmed its origin.

In two cases the phalangeal symptoms appeared six and eight weeks before the clinical signs of pulmonary involvement.

The cause for this unusual metastasis is thought to be the easy access of the bronchial growth to the pulmonary veins, thence to the systemic arteries.—*J. S. Summers, M.D.*

LENNON, WILLIAM, and CHALMERS, ISABELLA. Ankylosing spondylitis. *Lancet*, 1948, *1*, 12–15.

This is a report of 32 cases seen at the Rheumatic Unit, Royal Free Hospital, London, in a twelve month period. They found the commonest age of onset to be the third decade. One case started at 11 years of age, 6 cases at 15–20, 14 cases at 20–30, 9 cases at 30–40 years, 1 case at 40–50 years and 1 case at 50–60 years. These cases were of all types of physique and not necessarily confined to the virile athletic type as suggested by some writers. They could find no definite association between this disease and "septic foci."

The authors believe that the early roentgen changes in the sacroiliac joints are the key to early diagnosis even in the absence of clinical findings (2 cases). They find much relief of pain and stiffness from roentgen therapy, but can draw no conclusions as to its altering the ultimate course of the disease.—*J. S. Summers, M.D.*

BLOOD AND LYMPH SYSTEM

SYMMERS, DOUGLAS. Lymphoid diseases. *Arch. Path.*, Jan., 1948, *45*, 73–131.

This paper is an excellent review of the lymphoid diseases grouped into Hodgkin's disease, giant follicular lymphadenopathy, lymphoid leukemia, lymphosarcoma, and gastrointestinal pseudoleukemia of Briquet. There is an extensive discussion of the etiology, pathological aspects, symptoms and signs, diagnosis and treatment of each disease. The paper is recommended to the reader in the original. The author emphasizes that all these diseases are initiated by hyperplasia of the lymph follicles and that they are primary in the deep lymphoid structures, seen only in the superficial nodes as a late and secondary finding. The theories concerning the etiology and nature of Hodgkin's disease remain unsettled. Symmers is convinced that the majority of the evidence favors the disease as an infective process. The opposing view is that it is a primary cancer of lymph nodes. The author's theory includes that Hodgkin's disease is a process of myeloidization of lymphoid structure with embolism of megakaryocytes from the marrow as instigating factors. A related theory was advanced by Medlar in that Hodgkin's disease is a primary malignancy of the bone marrow with megakaryocytoblasts metastasizing to the lymphoid structure.

Giant follicular lymphadenopathy usually pursues a benign course for long periods. It is markedly radiosensitive throughout most of its course. Cases of transformation into Hodgkin's disease or lymphoid leukemia have been recorded with rapid terminal sequences.

The classical course of lymphoid leukemia remains remarkably constant in most cases. However, two general groups exist, namely (1) the lymph nodes are generally enlarged and the spleen remains normal or relatively so, and (2) the situation is reversed with a huge spleen and little lymph node enlargement.

The parallelism of lymphosarcomatous lesions in dogs caused by a virus is discussed with reference to human cases of lymphosarcoma. Lymphosarcoma presents a complex clinical picture and the cases are grouped into five categories: (1) involvement of paired organs, (2) superficial nodes in localized areas, (3) intrathoracic collections of lymphoid tissue with involvement of the thymus, (4) leukosarcoma which terminates in acute lymphatic leukemia, and (5) involvement of the lymphoid tissues of the abdomen including gastrointestinal tract and regional nodes—both retroperitoneal and mesenteric.

The cases of gastrointestinal pseudoleukemia of Briquet with marked lymphoid hyperplasia extending from the tongue throughout the gastrointestinal tract to the anus are regarded as a form of lymphosarcoma although they lack the infiltrative and destructive features of a true neoplasm.—*T. D. Allison, M.D., and C. L. Hinkel, M.D.*

GARDNER, L. B. Cooley's erythroblastic anemia in two Chinese boys. *J. Pediat.*, Sept., 1947, *31*, 347–354.

A few cases of Cooley's anemia have been reported in patients of families not native to lands adjacent to the Mediterranean Sea. One previous case has been reported in a Chinese child. The author reports 2 cases in Chinese boys.

The first patient was eight months old on first admission. Laboratory studies of the blood demonstrated typical erythroblastic anemia. Clinically the child showed pallor, a cardiac murmur, splenomegaly and hepatomegaly. The roentgen findings on first admission were not conclusive. A splenectomy was performed. On

the last admission of several, four years later, a definite increase in thickness of the frontal bones was demonstrable by roentgen ray as well as pronounced trabeculations of the bones of the hands.

The second case was a three year old Chinese male infant who exhibited marked pallor, splenomegaly and hepatomegaly. Roentgenograms of the skull showed thickening of the frontal area and generalized mottling of the calvarium. Roentgenograms of the hands showed cortical thinning and coarsening of the trabecular pattern. Laboratory studies showed erythroblastic anemia.—*Rolfe M. Harvey.*

Prinzmetal, M., Ornitz, E. M., Jr., Simkin, B., and Bergman, H. C. Arterio-venous anastomoses in liver, spleen, and lungs. *Am. J. Physiol.*, Jan., 1948, *152*, 48–52.

The authors utilize a technique previously described by them of arterial injection and venous recovery of microscopic glass spheres in studying arteriovenous anastomoses of various organs.

In the present experiments dogs, rabbits and cats were employed. Spheres injected into the portal vein, splenic artery, and right ventricle and pulmonary artery were recovered from the lungs, liver and splenic vein and liver and pulmonary vein respectively. The size of the recovered spheres of greater than the maximum capillary diameter was taken as a measure of the caliber of the arteriovenous shunts in the organs studied. These range from 50 to 180 microns in the liver, 160 to 380μ in the spleen and 100 to 390μ in the lungs.—*L. Feder, M.D.*

GENERAL

Cone, Ross B. A review of Boeck's sarcoid with analysis of twelve cases occurring in children. *J. Pediat.*, June, 1948, *32*, 629–640.

Boeck's sarcoid is a specific chronic infectious disease of unknown etiology which may affect any organ of the body, although commonly involving the skin, lymph nodes, eyes, salivary glands, lungs and bones of the hands and feet. The skin lesions show more chronicity than the extracutaneous lesions which tend toward spontaneous regression.

Among the theories as to etiology are an anergic form of tuberculosis, a mycobacterium and a virus. The microscopic picture strongly resembles tuberculosis. Central necrosis of the tubercles is rare. Acid fast bacilli are rarely found.

The onset of the disease is insidious, with skin or lymph node involvement in 50 per cent of the cases and mild fever. Among other systems involved by the disease, in addition to the skin and lymphatics, are the eyes, lungs, heart, central nervous system, gastrointestinal tract and bones. The author discusses the changes produced in each of these systems in some detail.

Ten to 20 per cent of patients have involvement of the small and long bones of the hands and feet. The roentgen changes consist of trabeculations and cyst formation with sharply punched out areas and little evidence of reaction in the surrounding bone.

The lung roentgen changes are of three types:

1. Peribronchial fibrosis and thickening, extending downward symmetrically into the lower lobes.
2. Soft infiltration in the mid-lung fields sparing the apices.
3. Areas resembling miliary tuberculosis.

Lymphadenopathy is often present in the tracheobronchial and mediastinal nodes.

The author summarizes the positive findings in a group of 12 children, affected with sarcoidosis, admitted to the Duke Hospital. Only 1 of the 12 cases failed to show the typical lung changes by roentgen ray. Fifty per cent had bone changes roentgenologically.—*Rolfe M. Harvey, M.D.*

Schwartzman, J., Maffia, A., Crusius, M. E., and Brunhoffer, A. Congenital toxoplasmosis. *J. Pediat.*, July, 1948, *33*, 66–73.

The *Toxoplasma* is a protozoan parasite which has an affinity for the central nervous system. It has not been frequently reported in humans. It has been found to cause an acute encephalitis in older children and pulmonary infections in adults, as well as the originally reported infantile cases. The infection may be acquired in utero. The typical case has the following characteristics:

1. Infection in utero or shortly after birth with symptoms at birth or shortly after.
2. Signs of central nervous system injury such as tremors, spastic contraction of the extremities, convulsions, microcephalus, hydrocephalus, and mental retardation.
3. Ocular signs, especially chorioretinitis.
4. Roentgen evidence of intracerebral cal-

cification, often bilateral, involving the cerebral cortex and basal ganglia.

5. Xanthochromia, round cell pleocytosis and high proteins in the cerebrospinal fluid.
6. Recovery of *Toxoplasma* from body fluids of mice or rabbits by direct smear or inoculation.
7. Demonstration of *Toxoplasma*-neutralizing antibodies in blood of infant or mother.

The pathological findings are those of focal areas of inflammation and necrosis with miliary granulomas tending to calcify. Therapy is not efficacious.

The authors report the case of a seventeen month old Negro infant suffering from weight loss and mental retardation. The head was microcephalic. A roentgenogram of the skull showed diffuse areas of calcification distributed intracerebrally. Ophthalmoscopic examination showed diffuse bilateral chorioretinitis. Laboratory tests were negative. This is the first case of toxoplasmosis reported in which dwarfism was present.—*Rolfe M. Harvey, M.D.*

STOUT, ARTHUR P. Mesenchymoma, the mixed tumor of mesenchymal derivatives. *Ann. Surg.*, Feb., 1948, *127*, 278–290.

While for a number of years data have been accumulating on specific cell types of mesenchymal neoplasms such as liposarcoma, synovial sarcoma, rhabdomyosarcoma, etc., there are other mixed tumors of mesenchymal derivatives which have received little attention. Most of these are believed to result from dysontogenesis.

The author suggests the name mesenchymoma for this group of tumors and divides them into benign and malignant. There have been reported a number of such malignant neoplasms in the urogenital tract and breast; but this paper points out they can readily occur elsewhere and describes 8 cases. These cases show a great range in histopathologic composition with 2 of the cases containing five mesodermal types of neoplasms. Early and extensive resection is necessary for these tumors as they are markedly radioresistant.—*T. D. Allison, M.D., and C. L. Hinkel, M.D.*

ROENTGEN AND RADIUM THERAPY

GRAHAM, VINCENT P., and MEYER, RALPH R. Experiences with nasopharyngeal carcinoma. *Radiology*, Jan., 1948, *50*, 83–91.

Twenty-six cases of carcinoma of the nasopharynx are reviewed. In 62 per cent superior cervical node metastases were present and in 56 per cent of all the cases there was involvement of the fifth and sixth cranial nerves. Recurrent middle ear disease was a frequent symptom.

In all cases the rhinoscopists were able to visualize a nasopharyngeal mass or ulcer. The lateral view of the nasopharynx was useful to demonstrate a soft tissue mass, but seldom showed bone destruction. In 17 of 24 cases stereoscopic verticomental basal or axial views of the skull showed varying degrees of destruction of the petrous apex and medial portion of the greater wing of the sphenoid. This bone destruction is believed to be due either to direct invasion of bone by tumor or to pressure atrophy. The great majority of such tumors are epithelial in origin.

The average patient received a calculated tumor dose of 5,000 r within forty days through two lateral nasopharyngeal fields, each of which received 3,600 r skin dose, and one anterior facial field which received 1,500 r skin dose delivered with 200 kv. (peak) irradiation. The large lateral parts which include the regional lymph nodes are usually reduced to a 10×10 or 6×8 cm. field when the course is half completed, unless these nodes are positive for disease in which case the fields remain large—10×20 cm.

Good palliation and prolongation of life was obtained in almost all cases and a five year cure was obtained in approximately 20 per cent. An occasional patient lives for ten to twelve years following the onset of disease.—*Howard R. Crews, M.D.*

LAING, DONALD R. The roentgen treatment of subacute sinusitis in children. *Radiology*, Jan., 1948, *50*, 52–56.

In children an upper respiratory infection lasting for more than five days requires investigation of the tonsils, adenoid tissue, paranasal sinuses and allergic tests. The tonsils may be inspected visually and nasal secretions stained for eosinophils. Adenoid infection is difficult to evaluate since this region is relatively inaccessible, especially in children. Sinus infection may frequently be detected by a single view of the sinuses and is a relatively simple diagnostic procedure.

Sinusitis in children is difficult to treat by the usual procedures, since children do not tolerate

nasal packs or antral irrigations. Nine hundred children believed to have subacute sinusitis were treated with irradiation. These patients were treated through an anterior port, 8 or 10 cm. in diameter with lead eye shields. The lung roots were treated through a posterior 8 or 10 cm. port if cough was a predominant symptom. Treatment was also administered to each lateral nasopharynx through a 7 cm. field if there was impaired hearing or a history of intermittent ear ache. These patients received three treatments to each area, 80 r per treatment at three day intervals with 140 kv. (peak) therapy.

Of 900 patients treated, 71 per cent were cured after one course. Fifteen per cent showed moderate improvement following the first course and 55 per cent of these were cured by a second course of treatment. Fourteen per cent responded poorly and it is believed that these patients suffer from undiagnosed allergy.—*Howard R. Crews, M.D.*

Beckstrand, Grant. Palliative procedures in advanced cancer of the mouth. *Radiology*, Jan., 1948, *50*, 10–17.

The palliative management of patients with advanced cancer of the mouth is discussed.

These patients require general medical care as well as local treatment directed towards the relief of pain and control of infection. Local procedures and general health measures are discussed in detail. Palliative irradiation should be used as an adjunct to general care primarily to combat infection and retard tumor growth. Intensive irradiation may defeat its purpose by producing a vigorous local reaction with systemic ill effects.—*Howard R. Crews, M.D.*

Erskine, Arthur W. The management of advanced cancer of the breast. *Radiology*, Jan., 1948, *50*, 7–9.

Advanced cancer of the breast is usually divisible into two distinct groups.

In the first group the disease is local and usually ulcerated with fixation to the chest wall with or without axillary disease. Surgery is preferred when there is a reasonable chance for cure. The primary tumor may be removed and the defect covered with skin from the unaffected breast or elsewhere. In patients past sixty or seventy these tumors may be treated successfully with irradiation; at least the patient may live out her normal life without unpleasant symptoms of advanced cancer. The most spectacular results of roentgen therapy are seen in such cases.

In the second group there are widely disseminated metastases with or without local ulceration. In such cases all hope for a permanent cure must be abandoned. Simple excision of the primary tumor is probably indicated if ulceration is present. Radiologists and surgeons should refrain from attempting extensive therapeutic procedures and confine their efforts to retard the spread of disease and to the relief of pain.

Castration is of great value in retarding the course of advanced cancer. Equally good results are produced by either surgical or irradiation induced castration.

Severe pain is usually due to bone lesions or to pressure on nerves. Roentgen therapy in small doses is of definite value in controlling pain. Opiates should be used when necessary.—*Howard R. Crews, M.D.*

Costolow, William E. Care of patients with advanced pelvic cancer. *Radiology*, Jan., 1948, *50*, 3–6.

Irradiation is the generally accepted treatment of cancer of the vagina and cervix and, in conjunction with surgery, of cancer of the fundus.

This paper is essentially a plea for careful radiation treatment and general management of patients suffering from pelvic cancer.

Intensive pelvic irradiation is a major therapeutic procedure and patients receiving such treatment should have the benefit of close cooperation of the family physician, radiation therapist, surgeon and urologist.

Pelvic inflammatory disease is the cause of the majority of complications and every attempt should be made to recognize and treat this complication before intensive radiation therapy is started.

The urinary tract should be thoroughly investigated before treatment since many patients with pelvic cancer have asymptomatic or unrecognized urinary complications.

Transitory irradiation reactions include proctitis and cystitis. These reactions respond to local medication. If severe, treatment may be temporarily discontinued.

Vesicovaginal and rectovaginal fistula and ureteral obstruction with resultant infection are invariably due to extension of pelvic cancer.

The neurosurgical procedures for the relief

of intractable pain are discussed. Such procedures are usually too formidable for the average case. Non-opiates and eventually opiates are recommended.—*Howard R. Crews, M.D.*

PUND, EDGAR R., NETTLES, J. B., CALDWELL, J. D., and NIEBURGS, H. E., Preinvasive and invasive carcinoma of the cervix uteri. *Am. J. Obst. & Gynec.*, May, 1948, *55*, 831–837.

Cervical squamous cell carcinomas usually begin in the endocervical canal at the junction of the stratified squamous and columnar epithelia. The source of these cancers is probably the endocervical basal cell whose location corresponds to that of the early cancer.

Three stages of cervical cancers are described: (1) preinvasive carcinoma; (2) covert invasive carcinoma; (3) overt carcinoma.

The term "preinvasive carcinoma" denotes carcinoma which is confined to the natural surfaces and which does not penetrate the underlying stroma.

Ultimately the preinvasive carcinoma becomes invasive. The invasion occurs either from a large surface of the endocervix or from a single focus. The early invasive carcinomas are not visible on vaginal examination and are therefore denoted as covert invasive carcinomas. Difference in average age of patients in the preinvasive and covert invasive groups suggests that the period of latency before the preinvasive carcinoma becomes invasive may average 6.5 years.

The overt carcinomas are readily suspected by vaginal examination. Since the authors have observed only 2 early carcinomas which were limited to the vaginal surface of the cervix, they conclude that the great majority arise from the junctional endocervix and are not evident until there is definite penetration and ulceration of the vaginal surface of the cervix.

From their study they believe that the majority of cancers of the cervix become obvious only after a period of time averaging five years from onset of invasion and eleven years after incipiency.

Concentration of effort should be directed toward detection of preinvasive carcinoma because therein lies the greatest opportunity for cure. It is important that biopsies include the junction of the squamous and columnar epithelia, and it should be emphasized that the existence of preinvasive carcinoma is frequently not detected by single biopsies. It is suggested that the endocervix and endometrial surface of the uterus be curetted before treatment is started to differentiate between preinvasive and covert invasive carcinoma.

The authors prefer to recommend irradiation for both covert invasive carcinomas and for overt carcinomas. They now recommend total abdominal hysterectomy in cases of preinvasive carcinoma with preservation of the ovaries in the young. At operation, if invasion is thought to be present, the uterus should be left in place, and, because irradiation will be subsequently used, surgical castration is recommended. Cauterization, conization, and amputation of the cervix as treatment for preinvasive carcinoma are discouraged.—*John R. Hannan, M.D.*

DRIPS, DELLA G. Ovarian dysfunction in young women treated with low-dosage irradiation. *Am. J. Obst. & Gynec.*, May, 1948, *55*, 789–798.

Since 1927 the author has been using low dosage roentgen irradiation for the "amenorrheic type" of ovarian dysfunction. In this type there is a tendency to larger than normal intervals between the menstrual periods and a decrease in the flow or complete absence of menstruation. Two distinct groups were recognized early in the study—one group had no complaints other than menstrual irregularity and a tendency to gain weight during periods of amenorrhea, and the other group had many complaints associated both with menstrual periods and their periods of amenorrhea. The symptomatology in the first group was considered to be secondary to pituitary failure and in the second group it was attributed to ovarian failure.

In pituitary failure the gonadotrophic hormone is usually not found in the urine, and when failure is complete there is, at least temporarily, an absence of estrogen. In cases of ovarian failure gonadotrophic hormone is found in greater than normal amounts and estrogen may or may not be found depending on the degree of failure.

Clinically cases of ovarian dysfunction due to pituitary failure outnumber those due to failure primary in the ovaries. There are two groups exhibiting pituitary failure—the one group has pituitary failure secondary to some general systemic disturbance and the other

group apparently has an endogenous pituitary dysfunction.

A normal basal metabolic rate is established with thyroid extract and cyclic administration of ovarian hormones, particularly estrogens, is attempted for several months before resorting to irradiation in the pituitary failure groups. The author recommends irradiation over each temporal region, centering over the pituitary, and two fields over the anterior abdomen, centering over each ovary. The technique used: 200 kv., 20 ma., 0.75 mm. Cu and 1 mm. Al filters, 50 cm. distance for five minutes. This represents approximately one-sixth of a skin erythema dose.

Response to low dosage irradiation has been best in the pituitary failure group, and the best results are attained when amenorrhea has been present less than six months because irreversible atrophy of the genital tract has usually not occurred.

In the cases of primary ovarian failure, thyroid extract, cyclic administration of estrogens and pelvic heat are used, and if these measures fail, low dosage irradiation is given and is limited to the ovaries. The technique of irradiation is otherwise the same as for primary pituitary failure.

The object of therapy in both groups is to establish more regular normal menses and to continue these until pregnancy can take place. One hopes also to relieve symptoms associated with abnormal menstruation. The results of low dosage radiation therapy in a group of 331 patients have been excellent. Low dosage irradiation is the best single method of treatment in cases of amenorrhea of more than one year's duration. Combined therapy—thyroid extract, estrogens and irradiation—has been somewhat more effective than low dosage irradiation alone. The author considers it unwise to treat women for sterility alone with low dosage irradiation.—*John R. Hannan, M.D.*

Johnston, James R., and Jacox, Harold W. Rectal hemorrhage following irradiation for carcinoma of cervix. *Am. J. Obst. & Gynec.*, May, 1948, *55*, 891–893.

Late intestinal complications following irradiation for pelvic malignancy are recognized and frequently anticipated. Degrees of damage to the distal colon vary from the mildest type causing simple proctitis, through stages of destruction terminating in atrophy, stenosis or perforation. These changes are often on a basis of telangiectasia or obliterative endarteritis. Rectal hemorrhage frequently responds to medical treatment and a colostomy is seldom required to control hemorrhage.

In the case reported by the authors, radiation treatment of the primary carcinoma of the cervix began in March, 1937. It consisted of 50 mg. focus of radium (details not known) applied for forty-eight hours (2,400 mg-hr.), and followed by a series of high voltage (200 kv., 0.5 mm. Cu) roentgen treatments. The patient received 1,600 r (air) to each of four pelvic portals 12 by 17 cm. in size over a period of sixteen days.

In September, 1937, a biopsy of the cervix showed papillary adenocarcinoma. Radium treatment was instituted and consisted of two 40 mg. capsules of radium (1 mm. platinum filter) tandem in cervix and fundus and four 10 mg. needles (0.5 mm. platinum) in the parametria for thirty hours, a total of 3,600 mg-hr. Ten days later a series of roentgen treatments was begun using the same technique as before and totalling 1,400 r to each of four portals over a period of fourteen days.

One year later severe rectal hemorrhage developed which ultimately required resection of the terminal large bowel. The resected specimen showed fibrosis with undifferentiated metastatic carcinoma in the submucosa. Thirteen months after resection of the rectum and distal sigmoid the patient developed a carcinoma of the ascending colon. Seven years after resection of this group the patient is well without evidence of recurrence of either neoplasm.—*John R. Hannan, M.D.*

MISCELLANEOUS

Graef, Irving, Karnofsky, David A., Jager, Val B., Krichesky, Boris, and Smith, Homer W. The clinical and pathologic effects of the nitrogen and sulfur mustards in laboratory animals. *Am. J. Path.*, Jan., 1948, *24*, 1–47.

The official War Department symbols designating the compounds under investigation are as follows:

H bis (β-chloroethyl) sulfide
HN_1 ethyl-bis (β-chloroethyl) amine
HN_2 methyl- bis (β-chloroethyl) amine
HN_3 tris (β-chloroethyl) amine
TL_{301} iso-propyl-bis (β-chloroethyl) amine

The results obtained in the study of HN_2 are presented in most detail, this compound being accepted as the prototype for this group of vesicants.

Dosage is expressed in terms of LD_{50}, an arbitrary statistical value. At this dosage 5 of 10 intoxicated animals may be expected to die.

The reported "clinical" effects were observed in mice, rats, rabbits and dogs.

There is an asymptomatic latent period of one to two days following LD_{50} doses of the nitrogen and sulfur mustards, during which time lymphatic injury is abrupt. The thymus, spleen and lymph nodes involute rapidly. There is a concomitant rapid reduction of the peripheral blood lymphocytes. The hemopoietic cells of the bone marrow show injury as does the epithelium of the small intestine.

Anorexia, weight loss and mucoid diarrhea follow the latent period, with death occurring in 72 to 144 hours. "The hemopoietic cells of the marrow disappear uniformly and the marrow becomes aplastic. The peripheral blood is severely leukopenic, due to a progressive fall in granulocytes. The red count falls slightly but reticulocytes disappear and it is evident that the production of hemopoietic cells has ceased. The small intestine is distended with fluid; and gastric stasis . . . is consistently present in small animals. From the pylorus to the cecum the small intestine shows inflammatory and degenerative changes, with hyperemia, edema of the villi, sloughing of the epithelium and metaplastic changes in the persisting and regenerating epithelium."

Rapidly occurring neurologic symptoms leading to death in one to forty hours follows large parenteral dosage. Convulsions, incoordination, tremors, weakness and dyspnea as well as parasympathomimetic activity occur.

Upper respiratory injury following gassing at LD_{50} concentrations is severe and prolonged with considerable systemic intoxication due to absorption.

Oral administration (the hydrochloride form of the compounds) produces the changes in the small intestine as noted above. A local protective action is apparently exerted by the presence of food in the gastrointestinal tract. Systemic intoxication occurs with absorption from the intestine.

Survival of animals following LD_{50} doses is characterized by gradual weight recovery, restoration of bone marrow and lymphoid tissue and a return of leukocytes in the peripheral blood. The lymphocytes return rapidly, the granulocytes more slowly. The diarrhea subsides and there is healing of the intestinal epithelium.

A distinct parallel exists between the delayed systemic effect of the nitrogen and sulfur mustards and that occurring after experimental roentgen irradiation.

Photomicrographs of representative tissue changes are appended.—*Victor Kremens, M.D.*

MALLET, LUCIEN. Radio-compteur pour particules ionisantes. (Counter for ionizing particles.) *J. de radiol. et d'électrol.*, No. 7–8, 1946, *27*, 359–361.

This short article describes a satisfactory counter for measuring alpha, beta and other ionizing particles. It should be of interest to those who are radiation physicists and who might be interested in constructing such a Geiger-Müller counter for themselves. A very adequate wiring diagram of the apparatus is shown. The stability of the counter is checked by a method using KCl, since potassium is a natural beta-ray emitter; a method using a uranium standard is also given. The technique for using the counter in measuring radioactivity (*a*) in a solution containing the radioactive substance, (*b*) in moist substances (radioactive viscera of experimental animals), and (*c*) in radioisotope separations is given. The sensitivity of the counter is of the order of 10^{-9} gr.—*William M. Loehr, M.D.*

SUBJECT INDEX TO VOLUME 60

(abs) = abstract (E) = editorial

Abdomen, echinococcus cysts of, 337
Abscess, cerebellar (abs), 850
formation and vaginal fistula, diverticulitis with (abs), 716
Achalasia of cardia, association of, with esophageal carcinoma (abs), 570
Actinomycosis of liver (abs), 716
Adenomyosarcoma, bilateral embryonal, of kidney (abs), 578
Adrenal cortex, carcinoma of (abs), 150
Air passages, upper, cancer of, 735
Allen, Lewis G., 1891–1948, obituary, 421
portrait, 421
American Board of Radiology, 279
American College of Physicians, announcement of 1949 session, 280
research fellowships of, 279
American College of Radiology, 691
American Radium Society, annual meeting of (E), 842
American Roentgen Ray Society, announcement of change of place for 1949 meeting, 559
annual meeting of (E), 105; (E), 543
Executive Council awards, 848
new officers elected at 1948 meeting, 559
1948 meeting, preliminary program, 115
1948 meeting, Scientific Exhibit, 550
1948 meeting, Section on Instruction, 119
1948 meeting, Technical Exhibit, 558
1949 meeting, 114
Anal canal, carcinoma of, statistics of Fondation Curie, Paris, 807
Anastomoses, arteriovenous, in liver, spleen and lungs (abs), 857
Anatomical studies on human tuberculosis (abs), 704
Anatomy, roentgen, of lung (abs), 565
Anemia, Cooley's erythroblastic, in two Chinese boys (abs), 856
pernicious, gastroscopic observations in (abs), 717
sickle cell, case of long standing, with marked bone changes, 251
Aneurysm, cardiac, in child aged seven (abs), 567
congenital arteriovenous, of renal artery (abs), 152
Angiocardiography utilizing photoroentgen apparatus with rapid film changer, 646
Angiofibroma, juvenile nasopharyngeal (abs), 700
Angiography, cerebral, additional approach to internal carotid artery for (abs), 143
cerebral, technique using dilute diodrast (abs), 140
Angioma, subarachnoid cervical, with cutaneous hemangioma of corresponding metamere (abs), 580
Ankle joint, traumatic instability of, 498
Anomaly, new, of aorta (abs), 566
Antibiotics, treatment of cerebellar abscess of excision with aid of (abs), 850
Aorta, new anomaly of (abs), 566
Arachnoiditis, recurrent, in dorsal spinal region (abs), 581
Army physical examinations, chest photoroentgenography in (abs), 703
Arneson, A. N., President of American Radium Society, 1947–1948, portrait opposite page 741
Arterial visualization, possible significance of, in diagnosis of placenta praevia (abs), 575
Arteriovenous fistula of lung (abs), 709
Artery, renal, congenital arteriovenous aneurysm of (abs), 152
Arthritis, degenerative, of hip joint, clinical and pathological observations in, 225
traumatic, cyst-like lesions of carpal bones associated with (abs), 282
Ascariasis, pulmonary (abs), 711
Asthma, bronchography in patients with (abs), 711
Atomic bombing of Hiroshima and Nagasaki, ocular lesions following (abs), 698
Energy Commission policy on production and distribution of isotope-labeled compounds, 431
Atresia, congenital, of small intestine in newborn (abs), 574
Atrophies, cerebellar, pneumoencephalography in diagnosis of, 293
Auricle, kymographic studies of function of (abs), 708
left, roentgenology of (abs), 854

Beryllium compounds pulmonary disease in workers exposed to, roentgen characteristics (abs), 705
Betatron, depth dose studies of roentgen radiation generated by, 158
techniques for application of, to medical therapy, 153
Biliary calculi "floating under water" (abs), 717
Biology, applications of radioactivity in (abs), 722
Biopsy in diagnosis of tumors of bone, limitations and erroneous indications of (abs), 720
Bladder, carcinoma of, 737
carcinoma, relation of transitional cell buds, Golgi apparatus and mitochondria to, 535
cutaneous metastases from vesical carcinoma of (abs), 579
irradiation reactions in (abs), 291
Body measurements, use of roentgen ray in, 664

BOECK'S SARCOID, review of, with 12 cases occurring in children (abs), 857
BONE changes, marked, case of long standing sickle cell anemia with, 251
formation, heterotopic, following suprapubic prostatectomy (abs), 584
lesions, calcium, phosphorus and phosphatase as aids in diagnosis of (abs), 720
limitations and erroneous indications of biopsy in diagnosis of tumors of (abs), 720
marrow, miliary tuberculosis of (abs), 854
metastases from cancer of breast, colloidal lead orthophosphate associated with deep roentgen therapy in, 193
roentgen aspect of certain lesions of (abs), 721
BONES, echinococcus cysts of, 338
sclerosis of, in Gaucher's disease, 246
BOOK REVIEWS
Cancer: Diagnosis, Treatment, and Prognosis. By Lauren V. Ackerman, and Juan A. del Regato, 432
Hodgkin's Disease and Allied Disorders. By Henry Jackson, Jr., and Frederic Parker, Jr., 432
Practical X-Ray Treatment. By Arthur W. Erskine, 433
Textbook of Endocrinology. By Hans Selye, 692
Congenital Malformations: A Study of Parental Characteristics with Special Reference to the Reproductive Process. By Douglas P. Murphy, 692
The 1947 Year Book of Radiology. Edited by Charles A. Waters and Ira I. Kaplan, 693
Dr. Samuel Guthrie—Discoverer of Chloroform; Manufacturer of Percussion Pellets; Industrial Chemist (1782–1848). By Jesse Randolph Pawling, 694
400 Years of a Doctor's Life. Collected and arranged by George Rosen, and Beate Caspari-Rosen, 695
BRAIN, schistosomiasis of, due to *Schistosoma japonicum* (abs), 437
BREAST, cancer, colloidal lead orthophosphate associated with deep roentgen therapy in bone metastases from, 193
cancer of, 738
cancer of, in male, secondary to estrogenic administration (abs), 438
cancer, surgical and radiation treatment of, 776
management of advanced cancer of (abs), 859
metastasis to, from cervical cancer (abs), 701
tumors, infrared photographic study of superficial veins of thorax in relation to (abs), 438
BRONCHIAL RUPTURE, importance of, in tuberculosis of endothoracic lymph nodes (abs), 143
traumatic, with occlusion, 448
BRONCHIECTASIS (abs), 854
retrocardiac, 219
BRONCHIOGENIC cysts of mediastinum (abs), 710
BRONCHOGRAPHY in asthmatic patients (abs), 711
BRONCHOPNEUMONIA, early pleural effusion in pulmonary embolism and (abs), 712
BRONCHOVASCULAR pattern of right upper lobe of fifty lungs, analysis of variations in (abs), 708
BRUCELLOSIS, pulmonary (abs), 568

CADE, SIR STANFORD, Janeway Lecturer, 1948, portrait opposite page 731
CALCIFICATION in obliterated ductus arteriosus of infant, 411
intracerebral, in microcephalic (abs), 850
nontuberculous pulmonary (abs), 568
of cardiac skeleton and coronary vessels in living, roentgen demonstration of, 642
CALCIFICATIONS, pulmonary, histoplasmin and tuberculin sensitivity in relation to (abs), 568
CALCIFIED omental fat deposits, roentgen significance, 612
CALCINOSIS, massive, with chronic renal insufficiency due to polycystic kidneys (abs), 152
CALCIUM as aid in diagnosis of bone lesions (abs), 720
CALCULI, pancreatic (abs), 717
ureteral, modern concepts of (abs), 719
CANCER, achievement of radium in fight against, 731
advanced, involving ear, treatment of, 750
advanced, of breast, management of (abs), 859
advanced, of genitourinary tract, use of inositol in (abs), 576
advanced, of mouth, palliative procedures in (abs), 859
advanced pelvic, care of patients with (abs), 859
cells in urine, detection of (abs), 577
cervical, with metastasis to breast (abs), 701
chemotherapy of (abs), 586
criteria for reporting end results in, 832
detection centers, their role in cancer control, 824
intrinsic, of larynx (abs), 701
of breast, 738
of breast, colloidal lead orthophosphate associated with deep roentgen therapy in bone metastases from, 193
of breast in male, secondary to estrogenic administration (abs), 438
of breast, surgical and radiation treatment of, 776
of cervix uteri, complications following use of low intensity, long radium element needles in treatment of, 788
of cervix uteri, precision dosage in interstitial irradiation of, 522
of cervix uteri, radon treatment of, 382
of cervix uteri, review of 296 cases, 368
of cervix uteri, study of five to eleven year end results, 389
of cervix uteri, theory as to cause of (abs), 147
of genitourinary tract, stained smears of cells exfoliated in urine in diagnosis of (abs), 577
of human prostate, heterologous growth of (abs), 579
of larynx, mortality in (abs), 564

of larynx, radiation therapy of (abs), 440
of lower lip, 763
of penis, treatment of, at Norwegian Radium Hospital, 801
of skin, 738
of thyroid (abs), 851
of tongue, 735
of tongue, irradiation in, 511
of upper air passages, 735
of uterus, 734
primary, of lung, 58
problem, medical symposium on, 562
Carcinoma, bronchogenic, phalangeal metastases in (abs), 855
esophageal, association of achalasia of cardia with (abs), 570
nasopharyngeal (abs), 858
of adrenal cortex (abs), 150
of anal canal, statistics of Fondation Curie, Paris, 807
of bladder, 737
of bladder, relation of transitional cell buds, Golgi apparatus and mitochondria to, 535
of cervix uteri, analysis of 790 cases, 387
of cervix uteri, rectal hemorrhage following irradiation for (abs), 861
of esophagus, with special reference to metastases and extensions (abs), 565
of large intestine (abs), 145
of larynx, methods and results of treatment (abs), 564
of prostate (abs), 579
of stomach (abs), 571; (abs), 572; (abs), 573
of stomach, its incidence and detection, 600
preinvasive and invasive, of cervix uteri (abs), 860
preinvasive, of cervix uteri (abs), 147
primary of ureter (abs), 719
rectal, heterotopic ossification in area of metastasis from, 507
uterine, metastases of, to central nervous system (abs), 582
vesical, of urinary bladder, cutaneous metastases from (abs), 579
Cardia, association of achalasia of, with esophageal carcinoma (abs), 570
Cardiospasm, surgical treatment of (abs), 714
Cardiovascular anomalies, congenital, diagnosis and surgical treatment of (abs), 707
Carotid artery, internal, additional approach to, for cerebral angiography (abs), 143
Carpal bones, cyst-like lesions of (abs), 282
navicular, styloidectomy of radius in surgical treatment of non-union of (abs), 282
Catlin mark, 430
Cell buds, transitional, relation of, to carcinoma of bladder, 535
Cells exfoliated in urine, stained smears of, in diagnosis of cancer of genitourinary tract (abs), 577
Central Ohio Radiological Society, 113
Cerebellar abscess, treatment of, by excision with aid of antibiotics (abs), 850
atrophies, pneumoencephalography in diagnosis of, 293
Cerebral angiography, additional approach to internal carotid artery for (abs), 143
angiography, technique using dilute diodrast (abs), 140
hydatid cysts, primary (abs), 850
ventricles, penetrating wounds of (abs), 699
Cervix uteri, cancer, complications following use of low intensity, long radium element needles in treatment of, 788
cancer of, review of 296 cases, 368
cancer of, with metastasis to breast (abs), 701
cancer, radon treatment of, 382
cancer, study of five to eleven year end results, 389
carcinoma, analysis of 790 cases, 387
postirradiation ulcerations of, 795
precision dosage in interstitial irradiation of cancer of, 522
preinvasive and invasive carcinoma of (abs), 860
preinvasive carcinoma of (abs), 147
rectal hemorrhage following irradiation for carcinoma of (abs), 861
theory as to cause of cancer of (abs), 147
Cheek, malignant tumors of, in children, 758
Chemotherapy of cancer (abs), 586
Chest, adult silent (abs), 705
infrared photographic study of superficial veins of, in relation to breast tumors (abs), 438
mass roentgen survey, in Philadelphia war industries (abs), 702
photoroentgenography in Army physical examinations (abs), 703
roentgen surveys, mass, community organization for (abs), 702
Children, malignant tumors of cheek in, 758
painful heels in (abs), 584
roentgen diagnosis of diffuse leukemic infiltration of kidneys in, 13
roentgen treatment of subacute sinusitis in (abs), 858
twelve cases of Boeck's sarcoid occurring in (abs), 857
young, treatment of hemangioma in, 182
Cholecystocolic fistula diagnosed by roentgen examination, 658
Cholecystography, new position for, 263
with priodax, kidney studies during, 505
Cholesteatoma in temporal bone, roentgen diagnosis of (abs), 438
Cholesteatomata of temporal bone (abs), 437
Chondromalacia of patella (abs), 288
Chondronecrosis, laryngeal, following roentgen therapy, 22
Chordoma of right frontal sinus (abs), 699
sacrococcygeal (abs), 720

Clinical use of radium, concept of, 741
Cobalt^{60}, applications of, in therapy, 816
Colitis, chronic nonspecific ulcerative (abs), 715
idiopathic ulcerative, treatment of, by means of "medical ileostomy" and orally administered protein hydrolysate (abs), 716
right-sided (regional) (abs), 146
Colloidal lead orthophosphate associated with deep roentgen therapy in bone metastasis from cancer of breast, 193
Colon, gallstone ileus associated with diverticulitis of, 86
Congenital atresia of small intestine in newborn (abs), 574
cardiovascular anomalies, diagnosis and surgical treatment of (abs), 707
coxa vara (abs), 287
cyst of spinal meninges as cause of intermittent compression of spinal cord (abs), 581
dislocation of patella (abs), 288
heart block in infant with associated multiple congenital cardiac malformations (abs), 567
toxoplasmosis (abs), 857
vascular ring, diagnosis and treatment of tracheal and esophageal obstruction due to (abs), 439
Coolidge, William D., Laboratory, dedication of, 690
Dr. William D., tribute to, 675
Coronary vessels, roentgen demonstration of, in living, 642
Coxa vara, congenital (abs), 287
Cranial vault, pulmonary roentgen manifestations of eosinophilic granuloma of (abs), 569
Curie, Marie, portrait opposite page 723
Pierre, portrait opposite page 723
Cyst, congenital, of spinal meninges as cause of intermittent compression of spinal cord (abs), 581
leptomeningeal, extensive erosion of base of skull from (abs), 141
-like lesions of carpal bones (abs), 282
solitary, of kidney (abs), 717
Cystitis, acute exudative, of undetermined etiology (abs), 151
Cystourethrography, use of new viscous water-miscible contrast medium, rayopake, for (abs), 148
visco-rayopake in (abs), 148
Cysts, bronchiogenic, of mediastinum (abs), 710
mediastinal (abs), 141
primary cerebral hydatid (abs), 850
pyelogenic renal (abs), 718

Deficiency pattern, small intestinal, non-vitaminic factors involved in production of (abs), 715
Dermatology, contact roentgen therapy in (abs), 291
Diaphragm, traumatic hernia of (abs), 713
Diodrast, dilute, technique of cerebral angiography using (abs), 140
Dislocation, congenital, of patella (abs), 288
Dislocations, distribution of, caused by parachute jumping (abs), 284
Diverticula, multiple tracheal (abs), 852
of duodenum and jejunum (abs), 574
Diverticulitis of colon, gallstone ileus associated with, 86
with abscess formation and vaginal fistula (abs), 716
Diverticulosis of gallbladder, 256
Dosage levels, effective, in interstitial radium therapy, 745
precision, in interstitial irradiation of cancer of cervix uteri, 522
Dose, depth, studies of roentgen rays for energy levels from 20 to 100 million electron volts, 158
Dosimetry, gamma-ray, new photographic material for, 175
Ductus arteriosus, obliterated, of infant, calcification in, 411
Duodenal bulb, roentgen study of benign tumor of (abs), 574
symptoms, nephroptosis producing (abs), 151
Duodenitis from roentgen viewpoint (abs), 573
Duodenum, diverticula of (abs), 574
prolapse of gastric mucosa through pyloric canal into (abs), 714
tuberculosis of, 315
Dysentery, acute, small intestinal motility in, 587
Dysplasia, osseous, of nails, 633
Dystrophy of nails, 633

Ear, treatment of advanced cancer involving, 750
Editorials
The annual meeting of the American Roentgen Ray Society, 105
Alfred Franklin Hocker, 1902–1948, 107
The radiologist considers Geiger counters, 270
The Registry of Radiological Pathology, 272
Thomas Raymond Healy, 1879–1948, 273
Hydrothorax in congestive heart failure, 419
Lewis G. Allen, 1891–1948, 421
Edwin Louis Rypins, 1903–1948, 423
Edwin S. Flarsheim, 1894–1948, 425
The annual meeting of the American Roentgen Ray Society, 543
Late sequelae following internal isotope irradiation, 679
Leopold Freund, 1868–1943, 683
Nelius Julian Nessa, 1880–1948, 685
The fiftieth anniversary of the discovery of radium, 839
The annual meeting of the American Radium Society, 842
Effect of irradiation on epiphyseal growth (abs), 442
Effusion, pericardial, clinical and roentgen diagnosis of (abs), 144

Electrocardiography, correlation of roentgen cardiac kymography with (abs), 853
Embolism, pulmonary, early pleural effusion in (abs), 712
pulmonary, without infarction, 460
Embryoma of kidney (abs), 149
Emphysema, spontaneous mediastinal (abs), 144; (abs), 569
End results, criteria for reporting, 832
Endometritis, characteristics of hysterosalpingograms in (abs), 576
Enterocolitis, nonspecific, 471
Epiphyseal growth, effect of irradiation of (abs), 442
Epiphysis, slipped, in adolescent hip (abs), 286
Epithelioma, extensive, of larynx, roentgen treatment, 29
Esophageal hiatal hernias of short esophagus type (abs), 713
hiatus hernia with inversion of stomach, 63
Esophagus, association of achalasia of cardia with carcinoma of (abs), 570
benign pedunculated tumors of, 466
carcinoma of, with special reference to metastases and extensions (abs), 565
congenital short, thoracic stomach produced by, and esophageal hiatus hernia (abs), 566
diagnosis and treatment of obstruction of, due to congenital vascular ring (abs), 439
Estrogens, cancer of breast in male, secondary to administration of (abs), 438
Extremity, lower, disturbance of longitudinal growth associated with prolonged disability of (abs), 289
normal lower, evaluation of phlebography of, 650
Eye, lesions of, following atomic bombing of Hiroshima and Nagasaki (abs), 698

Fat deposits, calcified omental, roentgen significance, 612
Fellowships of Registry of Radiological Pathology, 278
Femur, fracture of neck of, anatomical study of mechanics, pathology and healing of (abs), 287
Fibrosarcoma, synovial (abs), 854
Film changer, rapid, angiocardiography utilizing photoroentgen apparatus with, 646
Fistula, arteriovenous, of lung (abs), 709
cholecystocolic, diagnosed by roentgen examination, 658
vaginal, diverticulitis with abscess formation and (abs), 716
Flarsheim, Edwin S., 1894–1948, obituary, 425
portrait, 425
Fondation Curie, Paris, statistics of carcinoma of anal canal at, 807
Food-barium mixture, pyloric obstruction more accurately demonstrated by, 593
Foreign bodies in trachea, sign of (abs), 852
Fracture of femoral neck, anatomical study of mechanics, pathology and healing of (abs), 287
recurrent osteochondral, of patella (abs), 289
Fractures, distribution of, caused by parachute jumping (abs), 284
Monteggia (abs), 583
recent, intramedullary nailing of (abs), 855
ununited, cyst-like lesions of carpal bones associated with (abs), 282
Freund, Leopold, 1868–1943, obituary, 683
portrait, 683

Gallbladder, diverticulosis of, 256
Gallstone ileus associated with diverticulitis of colon, 86
Gallstones "floating under water" (abs), 717
Gamma-ray dosimetry, new photographic material for, 175
Gastric retention and gastric ulcer, 80
ulcer. See Peptic ulcer
Gastritis, post-irradiation, gastroscopic picture in, 360
roentgen signs of, 77
Gastroenterostomy, pouch formation following, 69
Gastrointestinal tract, relation of acute mucosal hemorrhages and ulcers of, to intracranial lesions (abs), 570
roentgen appearance of, during first day of life (abs), 714
Gastroscopic observations in pernicious anemia (abs), 717
picture in post-irradiation gastritis, 360
Gastroscopy in diagnosis of gastric cancer (abs), 571
Gaucher's disease, clinical and roentgen findings in case of, 490
exhibiting roentgenographic features of Legg-Perthes' disease, 490
sclerosis of bones in, 246
Geiger counters, radiologist considers (E), 270
Genitourinary tract, cancer of, stained smears of cells exfoliated in urine in diagnosis of (abs), 577
use of inositol in advanced malignancy of (abs), 576
Goiter, exophthalmic, radio-iodine in treatment of, 45
Golgi apparatus, relation of, to carcinoma of bladder, 535
Granuloma, eosinophilic, of mandible and cranial vault, pulmonary roentgen manifestations of (abs), 569
eosinophilic, of rib (abs), 852
Growth, longitudinal, disturbance of, associated with prolonged disability of lower extremity (abs), 289

Hamartoma of lung, roentgen significance of, 605
Head, undistorted vertical projections of, from lateral and posteroanterior roentgenograms, 414

Healy, Thomas Raymond, 1879–1948, obituary, 273
portrait, 273
Heart, aneurysm of, in child aged seven (abs), 567
block, congenital, in infant with associated multiple congenital cardiac malformations (abs), 567
disease, pulmonary (abs), 853
failure, congestive, hydrothorax in (E), 419
occult injuries to (abs), 853
roentgen demonstration of calcification of skeleton of, 642
roentgen differentiation between pericardial effusion and dilatation of (abs), 711
roentgen kymography of (abs), 853
Hebrew Medical Journal, twenty-first anniversary year of, 280
Heels, painful, in children (abs), 584
Hemangioma, cutaneous, of corresponding metamere, subarachnoid cervical angioma with (abs), 580
of kidney, roentgen diagnosis, 408
treatment of, in infants and young children, 182
Hemangiomas of mouth (abs), 585
Hemorrhage, rectal, following irradiation for carcinoma of cervix (abs), 861
Hemorrhages, acute mucosal, and ulcers of gastrointestinal tract, relation of, to intracranial lesions (abs), 570
Hemosiderosis of lungs, typical roentgen findings (abs), 705
Hernia, mediastinal lung, roentgen examination of, with reference to tomography (abs), 710
traumatic diaphragmatic (abs), 713
Hernias, esophageal hiatal, of short esophagus type (abs), 713
Hiatus hernia, esophageal, thoracic stomach produced by, and congenital short esophagus (abs), 566
hernia, esophageal, with inversion of stomach, 63
Hilum, densities of, simulating neoplasms (abs), 707
Hip, adolescent, slipped epiphysis in (abs), 286
joint, clinical and pathological observations in study of degenerative arthritis of, 225
Hiroshima, ocular lesions following atomic bombing of (abs), 698
Histoplasmin and tuberculin sensitivity in relation to pulmonary calcifications (abs), 568
Hydatid cysts, primary cerebral (abs), 850
disease and its roentgen picture, 331
Hydronephrosis, massive (abs), 578
Hydrothorax in congestive heart failure (E) 419
Hypernephroma, spontaneous disappearance of pulmonary metastases after nephrectomy for (abs), 569
Hyperostosis, infantile cortical (abs), 583
Hysterosalpingograms in tuberculous salpingitis and endometritis, characteristics of (abs), 576
I^{131}, clinical use of, 45
Ileus, gallstone, associated with diverticulitis of colon, 86
Infant, calcification in obliterated ductus arteriosus of, 411
newborn, roentgen appearance of gastrointestinal tract during first day of life (abs), 714
sternum in (abs), 583
Infants, treatment of hemangioma in, 182
Infarction, pulmonary embolism without, 460
renal (abs), 718
Infrared photographic study of superficial veins of thorax in relation to breast tumors (abs), 438
Injury, mechanism of, of 3,000 fractures and dislocations caused by parachute jumping (abs), 284
Inositol, use of, in advanced malignancy of genitourinary tract (abs), 576
Inter-American Congress of Radiology, third, announcement of, 559
Intervertebral disc, backward displacement of fifth lumbar vertebra in degenerative disease of (abs), 285
lesions, lumbar, roentgen diagnosis (abs), 582
Intestine, large, carcinoma of (abs), 145
small, in newborn, congenital atresia of (abs), 574
small, motility of, in acute dysentery, 587
small, non-vitaminic factors involved in production of deficiency pattern of (abs), 715
Intracerebral calcification in microcephalic (abs), 850
Intracranial lesions, relation of acute mucosal hemorrhages and ulcers of gastrointestinal tract to (abs), 570
Inversion of stomach, esophageal hiatus hernia with, 63
Ionizing particles, counter for (abs), 862
Irradiation, effect of, on epiphyseal growth (abs), 442
gastroscopic picture in gastritis following, 360
in cancer of tongue, 511
internal isotope, late sequelae following (E), 679
interstitial, of cancer of cervix uteri, precision dosage in, 522
low dosage, ovarian dysfunction in young women treated with (abs), 860
neuropathy following, 617
of gastric cancer (abs), 573
simultaneous disappearance of treated and untreated tumors after, 207
Islets of Langerhans, tumors of (abs), 145
Isotope irradiation, late sequelae following internal (E), 679
-labeled compounds, Atomic Energy Commission policy on production and distribution of, 431
Isotopes, artificially radioactive, applications of, in therapy, 816

Janeway Lecture, 1948, 731
Jejunitis acuta phlegmonosa, roentgen diagnosis of (abs), 715
Jejunum, diverticula of (abs), 574

Kidney, bilateral embryonal adenomyosarcoma of (abs), 578
echinococcus cysts of, 337
embryoma of (abs), 149
hemangioma of, roentgen diagnosis, 408
malignancy of (abs), 150
malignant tumors of (abs), 150
renal rickets and polycystic disease of (abs), 578
right, osteogenic sarcoma involving (abs), 718
roentgen signs of benign and malignant tumors of (abs), 577
solitary cyst of (abs), 717
studies during cholecystography with priodax, 505
tumors of (abs), 149
Kidneys in children, roentgen diagnosis of diffuse leukemic infiltration of, 13
infarction of (abs), 718
polycystic, massive calcinosis with chronic renal insufficiency due to (abs), 152
pyelogenic cysts of (abs), 718
Knee joint, *Salmonella suipestifer* infection of (abs), 288
Salmonella suipestifer pyarthrosis of (abs), 289
Kymography, roentgen cardiac (abs), 853
studies of function of auricle by (abs), 708

Laryngeal chondronecrosis following roentgen therapy, 22
Larynx, cancer of radiation therapy (abs), 440
carcinoma of, methods and results of treatment (abs), 564
mortality in cancer of (abs), 564
intrinsic cancer of (abs), 701
roentgen treatment for extensive epithelioma of, 29
Legg-Perthes' disease, a syndrome of many etiologies?, 490
Leptomeningeal cyst, extensive erosion of base of skull from (abs), 141
Leukemic infiltration, diffuse, of kidneys in children, roentgen diagnosis of, 13
Lip, lower, cancer of, 763
Lipiodol, annual awards for roentgenograms made with, for 1948, 848
Liver, actinomycosis of (abs), 716
anomalous lobe of, 486
arteriovenous anastomoses in (abs), 857
echinococcus cysts of, 331
Löffler's syndrome, relation of pulmonary ascariasis to (abs), 711
Los Angeles Radiological Society, 848
Lucite plombage in extrapleural pneumolysis, roentgenographic studies of, 51
Lung, arteriovenous fistula of (abs), 709
eosinophil, relation of pulmonary ascariasis to (abs), 711
hamartoma of, roentgen significance, 605
hernia, mediastinal, roentgen examination of, with reference to tomography (abs), 710
hydatid cysts of, 341
metastasis, solitary, surgical treatment of (abs), 709
primary cancer of, with special reference to apical lung tumors, 58
Lungs, analysis of variations in bronchovascular pattern of right upper lobe of fifty (abs), 708
arteriovenous anastomoses in (abs), 857
ascariasis of (abs), 711
brucellosis of (abs), 568
calcifications of, histoplasmin and tuberculin sensitivity in relation to (abs), 568
disease of, in workers exposed to beryllium compounds, roentgen characteristics (abs), 705
embolism of, without infarction, 460
hemosiderosis of, typical roentgen findings (abs), 705
localization of cavities in, by modified roentgenographic technique (abs), 704
nontuberculous calcification of (abs), 568
roentgen anatomy of (abs), 565
roentgen manifestations in, of an eosinophilic granuloma of mandible and cranial vault (abs), 569
spontaneous disappearance of metastases of, after nephrectomy for hypernephroma (abs), 569
Lymph nodes, endothoracic, importance of bronchial rupture in tuberculosis of (abs), 143
primary tuberculous foci without changes in (abs), 704
Lymphadenitis, mediastinal (abs), 707
Lymphoid diseases (abs), 856

Malformations, respiratory, types, causes and significance (abs), 703
Malignant disease, therapeutic use of radioactive elements in (abs), 585
Mandible, pulmonary roentgen manifestations of eosinophilic granuloma of (abs), 569
Mastitis, chronic, roentgen therapy in (abs), 440
Mastoiditis, chronic, roentgen picture of (abs), 700
Measurements, body, use of roentgen ray in, 664
Mediastinal emphysema, spontaneous (abs), 144
Mediastinitis, chronic tuberculous (abs), 707
Mediastinum, anterior, tumors of (abs), 852
bronchiogenic cysts of (abs), 710
cysts and tumors of (abs), 141
Medical therapy, techniques for application of betatron to, 153
Medicine, applications of radioactivity in (abs), 722
Medulloblastoma cerebelli, diagnosis, treatment and survivals (abs), 850
Meninges, spinal, congenital cyst of, as cause of intermittent compression of spinal cord (abs), 581

Mesenchymoma, mixed tumor of mesenchymal derivatives (abs), 858
Metastases, bone, from cancer of breast, colloidal lead orthophosphate associated with deep roentgen therapy in, 193
cutaneous, from vesical carcinoma of urinary bladder (abs), 579
from carcinoma of esophagus (abs), 565
of uterine carcinoma to central nervous system (abs), 582
phalangeal, in bronchogenic carcinoma (abs), 855
pulmonary, spontaneous disappearance of, after nephrectomy for hypernephroma (abs), 569
Metastasis from rectal carcinoma, heterotopic ossification in area of, 507
solitary lung, surgical treatment of (abs), 709
to breast from cervical cancer (abs), 701
Methyl methacrylate (lucite) plombage in extrapleural pneumolysis, roentgenographic studies of, 51
Micro-arteriography, 1
Microcephalic, intracerebral calcification in (abs), 850
Mitochondria, relation of, to carcinoma of bladder, 535
Monitor meter, 260
Monteggia fractures (abs), 583
Mouth, hemangiomas of (abs), 585
palliative procedures in advanced cancer of (abs), 859
Mucosa, gastric, prolapse of, through pyloric canal into duodenum (abs), 714
Mustards, nitrogen and sulfur, clinical and pathologic effects of, in laboratory animals (abs), 861

Nagasaki, ocular lesions following atomic bombing of (abs), 698
Nails, osseous dysplasia and dystrophy of, 633
Nasopharyngeal angiofibroma, juvenile (abs), 700
Nasopharynx, carcinoma of (abs), 858
diagnosis and treatment of tumors of (abs), 699
Necrosis, aseptic, cyst-like lesions of carpal bones associated with (abs), 282
Neoplasms of maxillary antrum, 736
Nephrectomy for hypernephroma, spontaneous disappearance of pulmonary metastases after (abs), 569
Nephroptosis producing duodenal symptoms (abs), 151
Nervous system, central, metastases of uterine carcinoma to (abs), 582
Nessa, Nelius Julian, 1880–1948, obituary, 685
portrait, 685
Neuritis, plantar digital (abs), 290
Neurofibromatosis with defect in wall of orbit (abs), 140
Neuropathy, post-irradiation, 617
Newborn, congenital atresia of small intestine in (abs), 574
North Carolina Radiological Society, 848
Northern California Radiological Club, 114
Norwegian Radium Hospital, treatment of cancer of penis at, 801
Nuclear physics, course in application of, 113

Oak Ridge Institute of Nuclear Studies announces new radioisotope courses, 690
Occlusion, traumatic bronchial rupture with, 448
Oklahoma State Radiological Society, 114
Omental fat deposits, calcified, roentgen significance, 612
Ophthalmology, evaluation of roentgen diagnosis in (abs), 699
Optimum prime factors, utilization of, in spot roentgenography, 135
Orbit, neurofibromatosis with defect in wall of (abs), 140
Osseous dysplasia and dystrophy of nails, 633
Ossification, heterotopic, in area of metastasis from rectal carcinoma, 507
Osteoarthropathy, hypertrophic, 232
Osteogenesis imperfecta (abs), 282
cystica (abs), 282
Osteogenic sarcoma, multiple, 623
Osteoid osteoma (abs), 283
Otolaryngology, evaluation of roentgen diagnosis in (abs), 699
Ovaries, dysfunction of, in young women treated with low dosage irradiation (abs), 860

Pain, roentgen therapy of (abs), 585
Pancreas, calculi of (abs), 717
Pancreatitis, acute, experimental study with special reference to roentgen therapy (abs), 722
Papanicolaou method, clinical appraisal of (abs), 577
Parachute jumping, mechanism of injury and distribution of 3,000 fractures and dislocations caused by (abs), 284
Patella, chondromalacia of (abs), 288
congenital dislocation of (abs), 288
recurrent osteochondral fracture of (abs), 289
Pathological considerations in cancer of stomach (abs), 572
Pelvimetry, standardized roentgen (abs), 575
Pelvis, advanced cancer of, care of patients with (abs), 859
Penis, cancer, treatment of, at Norwegian Radium Hospital, 801
Peptic ulcer and gastric retention, 80
Pericardial effusion, clinical and roentgen diagnosis of (abs), 144
roentgen differentiation between cardiac dilatation and (abs), 711
Peyronie's disease, radium treatment of (abs), 721
Phalangeal metastases in bronchogenic carcinoma (abs), 855

Philadelphia war industries, mass chest roentgen survey in (abs), 702
Phlebography of normal lower extremity, evaluation of, 650
Phosphatase as aid in diagnosis of bone lesions (abs), 720
Phosphorus as aid in diagnosis of bone lesions (abs), 720
Photofluorographic camera development, 114
equipment, standardization of (abs), 703
Photographic material, new, for gamma-ray dosimetry, 175
Photoroentgen apparatus with rapid film changer, angiocardiography utilizing, 646
Photoroentgenographic results, comparison of 4 by 5 inch and 70 mm. equipment in 1,713 cases (abs), 702
Photoroentgenography, chest, in Army physical examinations (abs), 703
Pituitary gland, irradiation of tumors of, 348
Placenta praevia, possible significance of arterial visualization, in diagnosis of (abs), 575
Plantar digital neuritis (abs), 290
Plasma cell tumors (abs), 283
Pleural effusion, early in pulmonary embolism and pneumonia or bronchopneumonia (abs), 712
transudates, unusual roentgen configuration associated with congestive failure (abs), 713
Pneumoencephalography, diagnosis of suprasellar tumors by, 213
in diagnosis of cerebellar atrophies, 293
Pneumolysis, extrapleural, roentgenographic studies of methyl metacrylate (lucite) plombage in, 51
Pneumonia, early pleural effusion in pulmonary embolism and (abs), 712
Pneumonias associated with epidemic respiratory infections (abs), 711
Pneumothorax, accidental extrapleural (abs), 711
spontaneous (abs), 569
Polycystic disease of kidney (abs), 578
Pouch formation following gastroenterostomy, 69
Priodax, kidney studies during cholecystography with, 505
Prostate gland, carcinoma of (abs), 579
heterologous growth of cancer of (abs), 579
Prostatectomy, suprapubic, heterotopic bone formation following (abs), 584
Pyarthrosis, *Salmonella suipestifer*, of knee joint (abs), 289
Pylorus, hypertrophic stenosis of (abs), 570
obstruction of, more accurately demonstrated by food-barium mixture, 593

Radioactive elements in malignant disease, therapeutic use of (abs), 585
iodine, clinical use of, 45
Radioactivity, applications of, in biology and medicine (abs), 722
Radioisotope courses at Oak Ridge Institute of Nuclear Studies, 690
Radioisotopes, courses in, 561
with increased activities, availability of, 430
Radiological pathology, registry of (E), 272
Radiologist, carcinoma of stomach from point of view of (abs), 571
considers Geiger counters (E), 270
Radiologists, suggested outline for training of, at qualified United States Naval Hospitals, 90
Radiology, role of, today, its responsibility and its import upon our life, 443
visit to American laboratories of, at close of war (abs), 441
Radium, achievement of, in fight against cancer, 731
concept of clinical use of, 741
element needles, low intensity, long, complications following use of, in cancer of cervix uteri, 788
fiftieth anniversary of discovery of (E), 839
fifty years of, 723
therapy, interstitial, effective dosage levels in, 745
Radius, styloidectomy of, in surgical treatment of non-union of carpal navicular (abs), 282
Radon treatment of cancer of cervix uteri, 382
vaseline ointment, preparation of, 836
work, accuracy in (abs), 721
Rectum, hemorrhage of, following irradiation for carcinoma of cervix (abs), 861
heterotopic ossification in area of metastasis from carcinoma of, 507
Registry of Radiological Pathology (E), 272
fellowships of, 278
Respiratory infections, epidemic, pneumonias associated with (abs), 711
malformations, types, causes and significance (abs), 703
Retrocardiac bronchiectasis, 219
Retroperitoneal region, neurologic disability following intensive roentgen therapy to, 617
Reynolds, Lawrence, President of the American Roentgen Ray Society, 1948–1949, portrait opposite page 443
Rheumatism, chronic vertebral (abs), 286
Rhinology, evaluation of roentgen diagnosis in (abs), 699
Rib, eosinophilic granuloma of (abs), 852
Rickets, renal, and polycystic disease of kidney (abs), 578
Rocky Mountain Radiological Society, 113, 430
Roentgen appearance of hydatid disease, 331
determination of activity of minimal pulmonary tuberculosis, accuracy of, 303
diagnosis in ophthalmology, rhinology and otolaryngology, evaluation of (abs), 699
ray, use of, in body measurements, 664
rays for energy levels from 20 to 100 mev., depth dose studies of, 158
signs of gastritis, 77

therapy, contact, in dermatology (abs), 291
therapy, deep, colloidal lead orthophosphate associated with, in bone metastases from cancer of breast, 193
therapy, laryngeal chondronecrosis following, 22
Röntgen, Wilhelm Conrad, tribute to, 96
Roentgenograms, lateral and posteroanterior, undistorted vertical projections of head from, 414
Roentgenography of sections of organs injected with radiopaque material, technique of, 1
spot, utilization of optimum prime factors in, 135
Roentgenology of left auricle (abs), 854
Rypins, Edwin Louis, 1903–1948, obituary, 423
portrait, 423

Salmonella suipestifer infection of knee joint (abs), 288
pyarthrosis of knee joint (abs), 289
Salpingitis, tuberculous, characteristics of hysterosalpingograms in (abs), 576
Sarcoma, multiple osteogenic, 623
osteogenic, involving right kidney (abs), 718
Schistosoma japonicum, schistosomiasis of brain due to (abs), 437
Schistosomiasis of brain due to *Schistosoma japonicum* (abs), 437
Sclerosis of bones in Gaucher's disease, 246
Seminoma of testis, roentgen therapy of, 39
Silicosis, evolution of lesions of (abs), 706
latent, and tuberculosis (abs), 706
Sinus, right frontal, chordoma of (abs), 699
Sinusitis, subacute, roentgen treatment of, in children (abs), 858
Skeletal age (Todd) substitute for, for clinical use (abs), 582
Skin, cancer of, 738
Skull, extensive erosion of base of, from leptomeningeal cyst (abs), 141
premature closure of sutures of (abs), 436
Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay, 430
Spinal cord, congenital cyst of spinal meninges as cause of intermittent compression of (abs), 581
Spine, chronic rheumatic lesions of (abs), 286
recurrent arachnoiditis in dorsal region of (abs), 581
Spleen, arteriovenous anastomoses in (abs), 857
echinococcus cysts of, 337
Spondylitis, ankylosing (abs), 856
Stenosis, hypertrophic pyloric (abs), 570
Sternum, infant (abs), 583
Stomach, carcinoma, incidence and detection, 600
carcinoma of (abs), 571; (abs), 572; (abs), 573
esophageal hiatus hernia with inversion of, 63
thoracic, produced by esophageal hiatus hernia and congenital short esophagus (abs), 566
tuberculosis of, 315
tumors of upper third of, 323
Styloidectomy of radius in surgical treatment of non-union of carpal navicular (abs), 282
Suprarenal cortical syndrome (abs), 150
Suprasellar tumors, diagnosis of, by pneumoencephalography, 213
Surgical aspects of carcinoma of stomach (abs), 572
Sutures, cranial, premature closure of (abs), 436
Synovialomas (abs), 854

Technique for roentgenography of sections of organs injected with radiopaque material, 1
modified roentgenographic localization of pulmonary cavities by (abs), 704
of simultaneous tomography, 668
Techniques for application of betatron to medical therapy, 153
Temporal bone, cholesteatoma in, roentgen diagnosis (abs), 438
cholesteatomata of (abs), 437
Tennessee Radiological Society, 114
Teratoma, malignant, of testis, roentgen therapy of, 39
Testis, roentgen therapy of malignant tumors of, 39
tumors of (abs), 579
Therapy, applications of artificially radioactive isotopes in, 816
Thyroid gland, cancer of (abs), 851
Thyroiditis (abs), 701
Tomography, examination of mediastinal lung hernia by (abs), 710
theory and technique of simultaneous, 668
Tongue, cancer of, 735
irradiation in cancer of, 511
Toxoplasmosis, congenital (abs), 857
Trachea, diagnosis and treatment of obstruction of, due to congenital vascular ring (abs), 439
multiple diverticula of (abs), 852
sign of foreign bodies in (abs), 852
Traumatic instability of ankle joint, 498
Tuberculin and histoplasmin sensitivity in relation to pulmonary calcifications (abs), 568
Tuberculosis, human, anatomical studies on (abs), 704
human, reinfection complex (abs), 704
latent silicosis and (abs), 706
miliary, of bone marrow (abs), 854
minimal pulmonary, accuracy of roentgen determination of activity of, 303
of endothoracic lymph nodes, importance of bronchial rupture in (abs), 143
of mediastinal nodes (abs), 707
of stomach and duodenum, 315
pulmonary, extrapleural pneumolysis procedures in, utilizing methyl methacrylate (lucite) spheres for maintenance of collapse, 51
survey, St. Louis County (abs), 702
Tuberculous lesions, atypical primary (abs), 703
Tumor, benign, of duodenal bulb, roentgen study of (abs), 574

"hypernephroid" (abs), 149
mixed, of mesenchymal derivatives (abs), 858
Tumors, apical lung, 58
benign pedunculated, of esophagus, 466
hilar densities simulating (abs), 707
malignant, of cheek in children, 758
malignant, of testis, roentgen therapy of, 39
mediastinal (abs), 141
of anterior mediastinum (abs), 852
of bone, limitations and erroneous indications of biopsy in diagnosis of (abs), 720
of breast, infrared photographic study of superficial veins of thorax in relation to (abs), 438
of islets of Langerhans (abs), 145
of kidney (abs), 149
of kidney, roentgen signs of benign and malignant (abs), 577
of nasopharynx, diagnosis and treatment of (abs), 699
of upper third of stomach, 323
pituitary, irradiation of, 348
plasma cell (abs), 283
simultaneous disappearance of treated and untreated, after irradiation, 207
suprasellar, diagnosis of, by pneumoencephalography, 213
testicular (abs), 579

Ulcerations, postirradiation, of uterine cervix, 795
Ulcers of gastrointestinal tract, relation of, to intracranial lesions (abs), 570
United States Naval Hospitals, qualified, outline for training of radiologists at, 90
Ureter, modern concepts of calculi of (abs), 719
primary carcinoma of (abs), 719
Urine, detection of cancer cells in (abs), 577
stained smears of cells exfoliated in, in diagnosis of cancer of genitourinary tract (abs), 577
Urography, intravenous, roentgen signs of stasis and ureterorenal suppression during (abs), 576
Urology award, 562
Uterus, cancer of, 734
disease of, reactions in bladder following irradiation for (abs), 291
metastases of carcinoma of, to central nervous system (abs), 582

Veins, superficial, of thorax in relation to breast tumors, infrared photographic study of (abs), 438
Ventilation, collateral, in man (abs), 709
Ventricles, cerebral, penetrating wounds of (abs), 699
Vertebra, fifth lumbar, backward displacement of, in degenerative disc disease (abs), 285
Visco-rayopake in cystourethrography (abs), 148

Wilms' tumor (abs), 149; (abs), 578
World War II, visit to American laboratories of radiology at close of (abs), 441
Wounds, penetrating, of cerebral ventricles (abs), 699

AUTHOR INDEX TO VOLUME 60

Abels, Jules C., 700
Abeshouse, B. S., 584
Abramson, W., 438
Ackerman, Alfred J., 256, 623
Ackerman, Lauren V., 432
Adams, G. D., 153
Adams, Raymond D., 581
Adams, W. Stirk, 699
Aebersold, Paul C., 558
Allen, E. Peter, 575
Allen, J. Garrott, 552
Almy, G. M., 153
Anderson, Katherine, 574
Andrews, J. Robert, 824
Anthony, D. H., 699
Archer, Vincent W., 593
Arendt, Julian, 711
Areneson, A. N., 741
Atkins, Joseph P., 448
Auerbach, Stewart H., 147
Aufses, A. H., 707
Ayre, J. Ernest, 147

Baarsma, P. R., 709
Baclesse, F., 440
Baer, P., 570
Bagley, C. E., 576
Bailey, O. T., 850
Barclay, A. E., 1
Barden, Robert P., 505
Barker, W. F., 850
Barnhard, Leonard, 282
Barr, Joseph S., 442
Beckstrand, Grant, 859
Beeler, Raymond C., 466
Belskie, Abram, 551
Bergman, H. C., 857
Bernhardt, R. W., 702
Bernstein, Arthur, 713
Berry, J. V., 151
Berry, N. E., 151
Biggs, A. D., 568
Birkelo, Carl C., 303
Blades, Brian, 709
Bloch, Robert G., 219
Block, Matthew H., 555
Bothe, Albert E., 535
Bourdon, Rene, 291
Bowler, J. P., 150
Boyden, Edward A., 708
Bradsford, Martin L., 141
Bradshaw, Howard H., 574
Brailsford, James, 720
Braund, R. R., 152
Breed, H. E., 158
Breed, J. Ernest, 382
Brodny, M. L., 148
Bronitsky, Jacob, 288
Brook, Ray, 704
Brooks, Frank P., 486
Brunhoffer, A., 857
Bunin, Joseph J., 709
Burford, T. H., 707
Burkholder, T. M., 152
Butchart, James B., 182

Cade, Stanford, 731
Caldwell, J. C., 860
Campbell, M. F., 578
Cappon, D., 850
Carson, M. J., 707
Castellano, Agustin, 557
Chalmers, Isabella, 856
Charlton, E. E., 158
Chatton, P., 565
Childe, Arthur E., 411
Chisholm, Tague C., 722
Christie, Arthur C., 675, 839
Chute, R., 577
Ciccone, Roy, 284
Clark, Elizabeth A., 568
Clerf, Louis H., 36
Cobb, Cully A., Jr., 140
Coleman, H. M., 289
Coley, Bradley L., 720
Coliez, Robert, 576, 716
Collins, James N., 466
Colson, G. M., 855
Cone, Ross B., 857
Cook, James C., 193
Cook, Orrin S., 557
Cooper, George, Jr., 593
Corrigan, Kenneth E., 193
Corscaden, James A., 522, 797
Costero, I., 706
Costolow, William E., 859
Cottentot, Paul, 291
Crabtree, E. G., 718
Crile, George, 701
Cristol, David S., 535
Crohn, Burrill B., 146
Crosbie, James, 552
Cross, Glen O., 580
Crusius, M. E., 857
Cutler, J. W., 702

Dailey, Morris E., 45
Dancoff, S. M., 153
Davies, Roberts, 702
Davis, E. D., 699
Davison, Charles, 582
Dayman, Howard, 706
de Abreu, Manoel, 668
Delario, A. J., 207
del Regato, Juan A., 432
Deming, Clyde L., 579
Desjardins, Arthur U., 29
DeStefano, George A., 852
Diamant, Marcus, 700
Dickie, H. A., 569
Dickie, Helen A., 568
Dickson, Roger W., 567
Dillon, Raymond A., 558
Dirken, M. N. J., 709
Dockerty, Malcolm B., 145
Donlan, Charlotte P., 511, 522
Dotter, Charles T., 555, 646
Draznin, S. Z., 490
Dreizen, Samuel, 582
Drips, Della G., 860
Drymalski, George W., 403
Dubowy, Jerome, 86

Ecker, Arthur, 143
Edwards, Jesse E., 553
Effler, Don B., 709
Ehrlich, Harry E., 700
Elgenmark, Olle, 705
Elghammer, Richard, 552
Eliason, E. L., 717
Elkin, William F., 702
Elliott, William J., 411
Ellis, F., 721
Elsasser, W. A., 414
Engelstad, Rolf Bull, 776, 801
Ennuyer, A., 807
Epstein, Bernard S., 144, 650, 711
Erbes, John, 570
Erich, John B., 564
Erskine, Arthur W., 433, 798, 859
Esguerra Gomez, Gonzalo, 96
Etter, Lewis E., 551
Ettman, I. K., 642

Fabricius, Bryan, 708
Fagin, I. Donald, 144
Fairbank, H. A. Thomas, 282
Fairchild, G. Cranston, 573
Farkas, Aladár, 287
Fenichel, Nathan M., 144
Figi, Frederick A., 29, 564, 585
Findlay, C. W., 439
Fineman, Solomon, 555
Firor, Whitmer B., 693
Fischer, Mario, 702
Fisher, D. F., 699
Fletcher, Gilbert H., 285
Flick, J. J., 698
Flink, Edmund B., 720
Foster, Sidney E., 246
French, J. Douglas, 581

Fricke, R. E., 721
Friedman, Paul S., 408

Gall, Edward A., 442
Gardner, L. B., 856
Garland, L. H., 853
Garlock, John H., 146
Gaston, E. O., 555
Gentil, Fernando, 720
Gianturco, Cesare, 550
Gilbert, R., 569
Gilbert, René, 585
Gillespie, H. W., 582
Glass, W. H., 715
Görgényi-Göttche, O., 143
Golden, Ross, 603
Golding, F. Campbell, 287
Goldman, Leonard B., 551
Goodrich, William A., 22
Gordon, Everett J., 289
Gordon, Joseph, 704
Gottlieb, Charles, 707
Gould, David M., 144
Gowdey, John F., 13
Graef, Irving, 861
Graham, A. P., 150
Graham, Vincent P., 858
Grain, R., 574
Greeley, Arthur V., 701
Greenfield, Maurice M., 617
Grossman, Burton, 552
Grout, J. L. A., 571
Grow, John B., 141
Gubergrits, A. Ya., 853
Gusberg, S. C., 522
Gutman, R., 573

Hadley, Lee A., 552
Hahn, P. F., 585
Hall, Bernard, 555
Hall, Marvin F., 466
Hall, Wendell C., 605
Hamer, H. G., 718
Hanson, A. O., 153
Hardisty, Norris M., 486
Hardt, Leo L., 717
Harrington, E. L., 836
Harrington, Stuart W., 713
Harris, Herbert W., 288
Hartnett, Leo J., 575
Harvey, N. A., 149
Harvey, W. A., 568
Hausfeld, K. F., 579
Havens, Fred Z., 564
Hayner, J. Clifford, 287
Hedberg, G. A., 702
Herbst, W. P., 576
Herdner, 583
Herger, C. C., 291
Hickel, R., 577
Hickel, Richard, 716
Higgins, C. C., 579, 719
Highsmith, George P., 714
Hightower, Felda, 574
Himmelstein, Aaron, 709
Hodes, Philip J., 448, 603
Hodgson, H. K. Graham, 437
Hodgson, John R., 600, 721
Hoffman, H. A., 578
Hoffman, Joseph G., 175
Holm, Harry, 718
Holt, John F., 612
Hornberger, Carl S., 175
Horwitz, Thomas, 225
Hovenanian, Michael S., 579
Howes, William E., 389, 763
Huber, Frank, 80
Hudson, T. R., 713
Huggins, Charles, 586
Hughes, E. S. R., 584
Hughes, Felix, 713
Huizinga, Eelco, 709
Hulbert, Bernard, 507
Huntington, Charles G., 80
Husebye, O. W., 715
Hynes, John F., 368

Ingraham, F. D., 140, 850
Irwin, Mary A., 702

Jackman, Raymond J., 145
Jackson, Henry, Jr., 432
Jacobson, Leon O., 555
Jacox, Harold W., 795, 799, 861
Jager, Val B., 861
Jaspin, George, 232
Jenkinson, David L., 658
Jennings, W. A., 721
Johnson, Julian, 448, 713
Johnston, James R., 861
Jolles, Benjamin, 745
Jones, John P., 567
Jordan, Hovey, 703
Joseph, Gerald F., 565

Kaplan, Gustave, 554
Kaplan, Ira I., 693
Karnofsky, David A., 861
Kassay, D., 143
Katterjohn, James C., 182
Kay, Earle B., 713, 714
Kearney, Edward A., 486
Keefer, George P., 440, 587, 604
Kelly, Harriet J., 582
Kerman, Herbert D., 51
Kerr, H. Dabney, 348
Kerst, D. W., 153
Kestler, Otto C., 498
Kirklin, B. R., 263, 600, 604
Kirsner, Joseph B., 715
Kisner, Wendell, 574
Kjellberg, Sven Roland, 705, 852
Klosk, Emanuel, 713
Knutsson, Folke, 854
Koch, H. W., 153
Koiransky, H. G., 642
Kretschmer, H. L., 578
Krichesky, Boris, 861
Kurtzhalz, Charles, 702

Lachapèle, A. P., 286
Laing, Donald R., 858
Lamarque, P., 441
Lame, Edwin L., 557
Landau, George M., 705
Landy, Ernest, 69
Lanzl, E. F., 153
Lanzl, L. H., 153
Laughlin, J. S., 153
Lawson, Robert B., 574
Leddy, Eugene T., 39
Lennon, William, 856
Lenz, Maurice, 22, 38, 541, 842
Lepennetier, F., 574
Lerner, Henry H., 251
Leucutia, T., 193, 543, 679
Lewis, L. C., 579
Lilja, Bengt, 700
Lingley, James R., 442
Lipin, Theodore, 582
Little, Samuel C., 437
Livinstone, Robert G., 633
Lloyd, Milton S., 852
Loewe, Leo, 650
Lomhoff, Irving I., 86
Lopez-Kruger, Rodolfo, 145
Lowry, Harvey M., 658
Lumb, George, 283

MacArthur, Robert A., 556
Macdonald, Eleanor J., 832
McDonald, John R., 554
McGraw, W. H., 551
Machella, Thomas E., 716
MacIntyre, Robert S., 612
McKeen, Charles L., 552
McLaughlin, W. L., 150
MacMillan, R. L., 152
McNabb, A. M., 135
Macpherson, Margaret, 703
Macy, Icie G., 582
Maffia, A., 857
Mahon, Hugh W., 141
Mahorner, Howard, 574
Maier, Herbert C., 709, 710
Maleki, A., 565
Malenchini, Manuel, 323
Mallet, Lucien, 862
Manganiello, Louis O. J., 664
Mann, Arvin W., 582

Mann, L. T., 569
Manning, Isaac Hall, Jr., 714
Marck, A., 714
Marks, E. K., 555
Marks, Joseph H., 63
Marshak, Richard H., 716
Marshall, V. F., 577
Martin, Charles L., 750
Martin, Hayes, 700
Martin, James A., 750
Martin, Paul H., 286
Massopust, Leo C., 438
Mauer, Elmer, 852
Meade, R. H., 713
Meyer, Ralph R., 858
Meyers, Solomon G., 288
Miller, Earl R., 45
Miller, T. Grier, 716
Mino, Robert A., 633
Mino, Victor H., 633
Mitchell, Earl B., 219
Moberg, Gunnar, 712
Moore, Sherwood, 430, 550
Morgan, Russell H., 144, 556, 703
Morgan, W. G., 558
Morin, G., 574
Mulkley, J. W., 551
Mumford, E. B., 288
Murphey, Francis, 437
Murphy, Douglas P., 692
Murphy, William P., Jr., 558
Myers, William G., 816

Negus, V. E., 701
Neibling, Harold A., 145
Nettles, J. B., 860
Neuhauser, Edward B. D., 13
Neuhof, H., 707
New, Gordon B., 564
Newton, Isaac L., 135
Nieburgs, H. E., 860
Nielsen, Karen, 852
Nissen, K. I., 290
Nolan, James F., 175

Olsan, Edwin S., 471
Olson, Arthur M., 713
Olsson, Olle, 711
O'Neill, James F., 574
Ornitz, E. M., Jr., 857
Ostrum, Herman W., 315, 557

Palmer, Eddy D., 360
Palmer, Walter Lincoln, 715
Parker, Frederic, Jr., 432
Parsonnet, Aaron E., 713
Pascucci, Lucien M., 705
Paul, R. N., 566
Pawling, Jesse Randolph, 694
Pearse, R., 152
Pendergrass, Eugene P., 182, 540, 557
Pennybacker, Joe, 850
Pereiras, Raul, 557
Peterson, Harold O., 555
Peyton, W. T., 140, 436
Pfahler, George E., 440, 798
Phemister, Dallas B., 282
Phillips, Gilbert, 850
Pomeroy, Lawrence A., 387
Portmann, U. V., 799
Prinzmetal, M., 857
Prosser, T. M., 283
Pugh, David G., 721
Pund, Edgar R., 147, 860
Putney, F. Johnson, 566
Pyle, S. Idell, 582

Quastler, H., 153
Quick, Douglas, 37
Quimby, Edith H., 723

Rague, Paul O., 303
Regan, F. C., 718
Reidy, John A., 442
Reyersbach, G. C., 439
Reynolds, Lawrence, 193, 443
Richards, C. E., 148
Richards, Charles M., 799
Richards, Gordon E., 541
Richman, Robert M., 284
Ricketts, William E., 715
Riesen, D. E., 153
Rigby, R. C., 568
Rigler, Leo G., 460, 555
Riley, Richard L., 709
Roach, John F., 556
Robins, S. A., 148
Robinson, C. S., 153
Roca, Jaime, 323
Rodgers, H. W., 571
Rodholm, A. K., 282
Rosen, George, 695
Rosenstein, Joseph, 763
Ross, Donald, 289
Roswit, Bernard, 554
Roulhac, George E., 699
Roux-Berger, J. L., 807
Roy, Wallace M., 557
Rubenfeld, Sidney, 693
Russ, S., 721

Sachs, M. D., 551
Salinger, Hans, 710
Sanchez-Perez, J. M., 550
Sandock, Louis F., 219
Sauer, H. R., 291
Saunders, Bernard G., 558
Scadding, J. G., 711
Scannell, J. Gordon, 708
Schaefer, Arthur A., 570
Schechter, Samuel E., 507
Schiller, Israel A., 703
Schlanger, Henriette, 331
Schlanger, Pablo M., 331
Schleicher, Emil Maro, 854
Schlezinger, N. S., 213
Schmidlapp, C. J., II, 577
Schoenberger, A. P., 579
Schoolman, Joseph G., 564
Schorsch, Hildegarde A., 705
Schwab, Edward H., 144
Schwartz, Henry G., 699
Schwartz, Steven O., 717
Schwartzman, J., 857
Scott, Wendell G., 90, 550
Seibel, Roy E., 722
Selye, Hans, 692
Senturia, Hyman R., 507
Serber, William, 315
Shapiro, Robert, 460
Sharlin, H. S., 707
Sharpe, A. M., 702
Shechter, Nathan, 289
Sheppard, C. W., 585
Sherman, Jerome, 711
Sherman, Mary S., 283
Shipley, E. Roderick, 758
Shorter, Alan, 573
Shorvon, L. M., 716
Shuman, H. H., 583
Sicher, K., 570
Siguier, 574
Silver, H. K., 149
Simkin, B., 857
Simmons, D. R., 140, 436
Simmons, E. L., 555
Simpson, Frank E., 382
Singer, Jacob J., 854
Singer, Karl, 490
Skaggs, L. S., 153
Sloan, Robert D., 556
Smith, Frederick M., 583
Smith, Homer W., 861
Smith, R. A., 717
Snedden, H. E., 551
Sodeman, W. A., 853
Soley, Mayo H., 45
Solis-Cohen, Leon, 408
Sosman, Merrill C., 358
Soule, Arthur B., Jr., 141
Speert, Harold, 701
Spies, Tom D., 582
Stark, Frederick M., 617
Steigmann, Frederick, 717
Stein, Justin J., 58
Steinberg, Israel, 555, 646
Stewart, Matthew J., 572
Stock, F. E., 719
Stout, Arthur P., 858

Strassmann, George S., 570
Strohl, A., 722
Stubbins, Sam G., 282
Sun, Ko-Chi, 576
Sussman, Marcy L., 471
Sweany, Henry C., 403
Sweet, R. H., 439
Swenson, Paul C., 602
Symmers, Douglas, 856

Taft, Robert B., 260, 270
Taquino, George J., 565
Taylor, Hermon, 572
Tellman, H. C., 556
Temple, Harold L., 232, 555, 646
Teplick, J. George, 213
Terplan, Kornel, 704
Thomas, S. F., 853
Thompson, J. Robert, 403
Tice, Frederick, 702
Tracy, E. M., 788

Uzman, L., 293

Van Allen, Willard W., 114, 703
van der Sar, 711
Van Duzen, R. E., 151
Varney, J. H., 721
Vaughan, Luther M., 29
Vivas-Salas, E., 567
Voluter, G., 569

Wald, B., 854
Walk, L., 77
Walzer, Eugene E., 711
Ward, Grant E., 758
Ward, R., 851
Warden, J. G., 719
Warshawsky, H., 438
Wasch, M. G., 650, 714
Waterman, G. W., 788, 799
Waters, Charles A., 693
Watson, Charles W., 437
Watson, E. M., 291
Waugh, John M., 145
Wear, J. B., 579

Wegner, Walter, 581
Weil, Inga F., 251
Weintraub, Syndey, 556
Welin, Sölve, 438
Wells, C., 719
Welty, R. F., 717
Westerhorn, Anders, 855
Whipple, Harry O., 175
Whitcomb, Benjamin B., 140
Willcox, A., 855
Williams, D. W., 577
Williams, Robert G., 556
Wilson, Milton J., 287
Windholz, Frank, 246
Wishard, W. N., 718
Wood, J. W., 702
Woolner, Lewis B., 554
Wylie, Wendell L., 414

Yarnis, Harry, 146
Yiannacopoulos, Apostalos, 557
Young, H. Herman, 721

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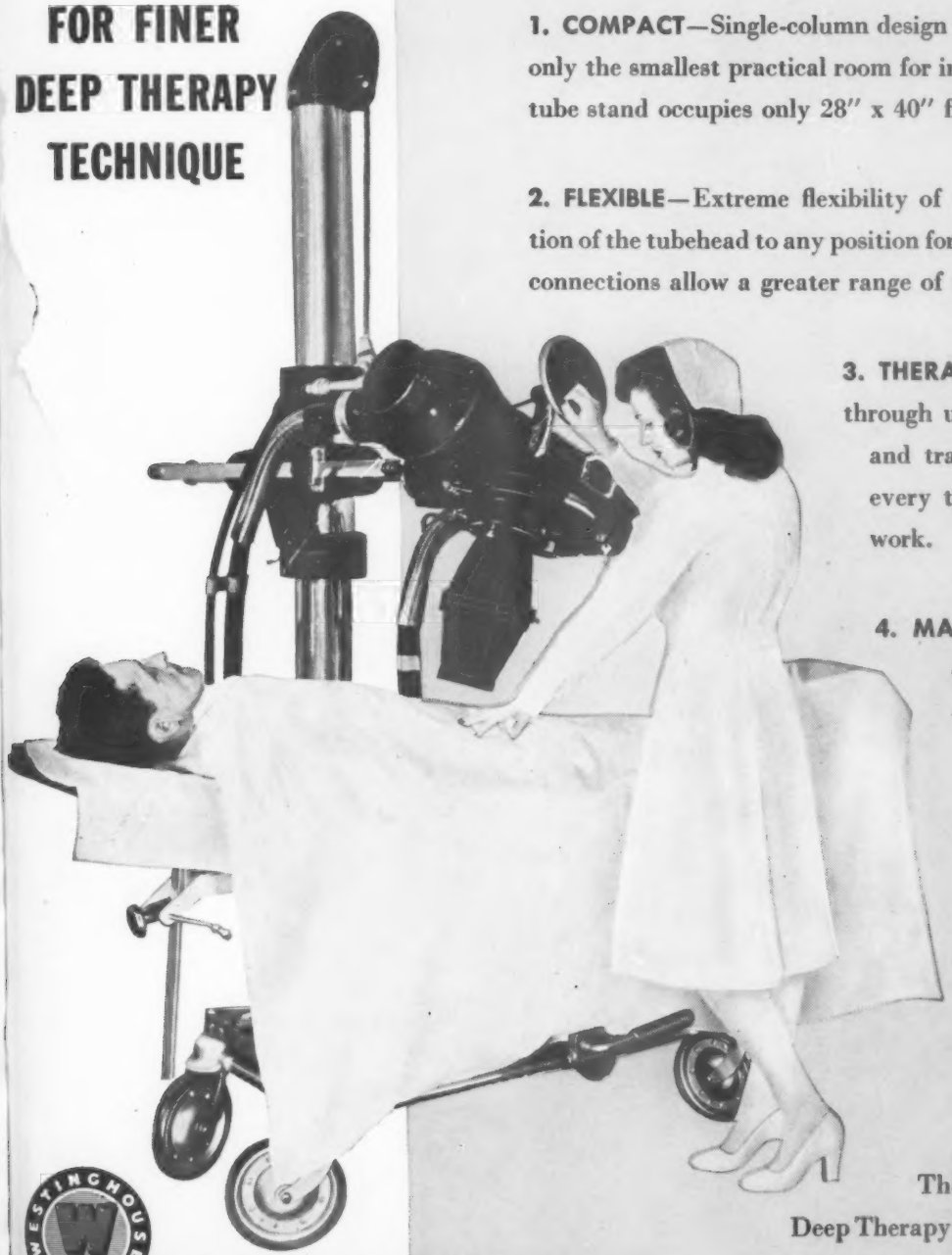

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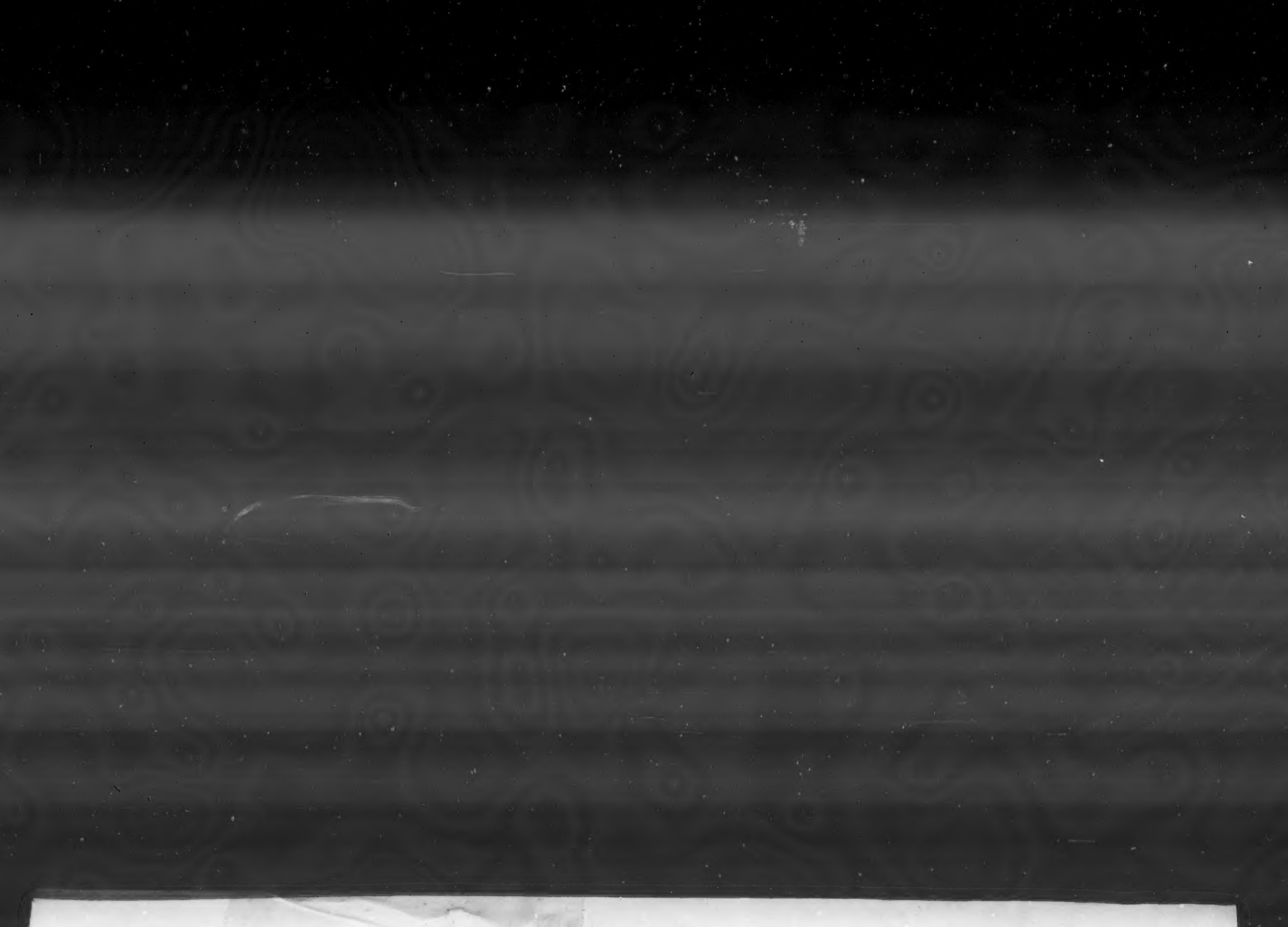
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